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EXTINCTION AND PRECIPITATION OF CUTANEOUS SENSATIONS

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It is generally assumed that the cutaneous modalities of one side of the body are represented in the opposite side of the brain. Conventionally, a lesion in the right parietal lobe causes a decrease in sensation on the left side of the body. However, there is also clinical and physiologic evidence indicating that certain parts of the body are bilaterally represented in the parietal cortex. Foerster [1] electrically stimulated the sensory cortical area in man, with the result that the patient complained of bilateral paresthesias. Dusser de Barenne [2] reported that painting a small part of the arm area in one parietal cortex with strychnine produced hypersensitivity in both arms in the monkey. Other than these investigations, there are relatively few studies demonstrating a functional relationship between the sensations of the two halves of the body, such as stimulation of the skin on one side influencing the cutaneous sensation on the opposite side of the body.

In a previous communication, a competitive relationship between the visual sensation in the right and that in the left homonymous fields was described.[3] One side was found to influence the other, and it was hypothesized that the healthy side dominated and inhibited the diseased side. In a patient who survived a gunshot wound of the left occipitoparietal cortex, it was found that when visual stimuli were simultaneously exposed on the two sides of a fixation point he perceived the image on the left side, while the image on the right appeared dull and obscure or became totally extinct. When the object in the normal field was removed, he clearly perceived the object remaining in the affected field of vision. Furthermore, it was noted that the more visual stimulation there was on his left side, the less he saw in the right field of vision. The phenomena of visual obscuration and extinction described illustrate a functional relationship between the two occipital lobes. Now, if such phenomena are demonstrable in the visual perceptive spheres, it is reasonable to assume that they should also be found on testing the cutaneous modalities under the same conditions. As a matter of fact, Oppenheim,[4] in 1900, casually mentioned the phenomenon in describing a method for sensory examinations, stating:

> In certain brain diseases which cause unilateral disturbance of sensibility the following procedure is advantageous. Stimulate simultaneously two symmetrical points. The patient will always detect it only on the sound side, whereas in single tests he may detect every stimulation of the affected side. The manner of examination, we would call the method of double stimulation.

From these observations it is apparent, then, that the phenomena of obscuration and extinction should be generally applicable to most forms of sensation. With this in mind, groups of patients with cutaneous sensory disturbances due to lesions at different levels of the nervous system were studied. The object of the investigation was to determine the nature and degree of sensory dulling or extinction with the method of double stimulation and to learn with what types of lesions these functional disturbances could be obtained. While the study was in progress, another group of patients was found in which a stimulus on the normal side precipitated or aggravated a burning pain on the opposite, or affected, side. The pain in the affected side was limited to the palm and fingers or to the sole and toes in a limb which was causalgic as a result of a nerve injury.

MATERIAL AND METHOD

Patients with gunshot wounds of the brain, spinal cord, nerve roots or peripheral nerves were studied. For obvious reasons, only subjects with a clear mind, good orientation and reasonable intelligence were considered. Whenever it seemed indicated, special tests of memory, retention, reasoning ability and imagination were given to determine the presence or absence and, if present, the degree, of intellectual impairment.[5] Many of the patients were studied over prolonged periods, and the changes in restitution of function were recorded. Special attention was given to: (1) the sensory response to "double stimulation" with mixed and uniform types of stimuli; (2) the temporal factors

1. Foerster, O., cited by Dusser de Barenne.[2]

2. Dusser de Barenne, J. G.: Central Levels of Sensory Integration, A. Research Nerv. & Ment. Dis., Proc. **15**:274, 1935.

3. Bender, M. B., and Furlow, L. T.: Phenomenon of Visual Extinction in Homonymous Fields of Vision and Psychological Principles Involved, Arch. Neurol. & Psychiat. **53**:29 (Jan.) 1945.

4. Oppenheim, H.: Diseases of the Nervous System, translated by E. E. Mayer, Philadelphia, J. B. Lippincott & Co., 1900, p. 59.

5. These tests were performed by Lieut. Comdr. A. L. Benton, H-(V)S, U.S.N.R.

in sensation, such as (*a*) sensory adaptation time,[6] (*b*) duration of after-sensation and (*c*) rate of fluctuation of sensation, and (3) spatial factors in cutaneous sensibility, such as (*a*) graphesthesia, or the ability to perceive figures drawn on the skin, (*b*) perception of direction of lines drawn on the skin and (*c*) ability to localize points touched or otherwise stimulated on the skin.

In eliciting the response to double, or simultaneous, cutaneous sensory stimulation, care was taken to insure that the applied stimuli were of equal strength. In a few instances the two points of a compass were simultaneously applied to each of the two corresponding parts of the body, the points being equally distant from the midline. For testing pain modality in most cases, graduated algesiometers, from 2.5 to 25 Gm., with a no. 10 needle point were used. For tactile sensation, small wisps of absorbent cotton were applied to the skin. Thermal sensibility was tested with small cold or warm metal objects. For vibration sense, a tuning fork of 128 vibrations per second was used. Other sensations tested were discrimination of weight, stereognosis and two point discrimination. Graphesthesia was elicited by writing with a pencil on the skin the number *4*, the letter *E*, a triangle, a circle and a square. With the double stimulation method, an image was drawn on one side and a few nondescript lines were simultaneously drawn on the other side of the body. The time relations for sensory adaptation, after-sensation and fluctuation in sensation were measured in seconds with a stopwatch.

REPORT OF CASES

CEREBRAL LESIONS

Case 1.—N. G. K., a Marine veteran aged 29, was admitted to the hospital in May 1944 because of dizzy spells and convulsive seizures. In 1936, he was accidentally shot, and the bullet lodged in the right side of his brain. There was immediate left hemiplegia, which subsequently receded. One year after injury, there appeared spells of falling and unconsciousness; despite this, he was able to work as a laborer until a few weeks prior to the present admission to the hospital, when the attacks became more frequent and severe.

Physical examination gave essentially normal results. There was a bony defect in the right parietal bone. Neurologic examination disclosed left hemiparesis with moderate spasticity involving mostly the distal portions of the arm and leg, concomitant signs referable to the pyramidal tract and noticeable atrophy of the affected extremities. In addition, strong clenching of the right fist caused involuntary flexion at the left hand and elbow, flexor movement at the knee and foot and sometimes spasm of the face. The functions of the cranial nerves were essentially normal except for diminished taste sensation on the left side. The visual acuity, visual fields and tachistoscopic perception were normal.

Sensation.—The patient complained that occasionally he did not know the whereabouts of his left hand, that the left side of his body felt numb and that he was unable to detect objects with his left hand.

The sensory defects were limited to the left side of the body. Pain and temperature sensations were reduced on that side, especially in the distal portions of the extremities. The response to painful stimulation varied. Frequently, the patient perceived a distinct point, but this sensation did not last long. During continual application of a 15 Gm. stimulus on the left forearm, the pain changed to a dull pressure sensation within two seconds, and the latter disappeared entirely within seven seconds. In the corresponding area on the right side, the same stimulus produced sense of pain for fifteen seconds and sense of pressure for over sixty seconds. In other words, the sensory adaptation time was greatly reduced on the affected side, especially in the distal portions of the extremities. As compared with the normal side, the adaptation time for pain and touch modalities was much shortened on the affected side, the sensations lasting only one second or disappearing immediately. Superficial tactile sense was diminshed over the same distribution as pain and temperature modalities. Fine tactile sense was absent over the left extremities, especially in the distal portions, and it was variably diminished over the trunk and the face. Vibration sense was preserved, whereas the senses of position and initiation of movement were lost completely in these limbs. The patient was unable to detect gross movements of the fingers or slow movement at the wrist and made errors in appreciation of the posture of the forearm. Stereognosis was lost in the affected hand, foot and side of the mouth. He was unable to detect the presence of a cigaret or to recognize objects with the left side of the lips as well as he did with the right side. Point localization was slightly impaired. He was unable to determine the direction or the type of lines drawn on the skin over the distal parts of the extremities. All he perceived was a movement associated with the deep pressure sense. He had pronounced agraphesthesia in these zones. Over the trunk he was sometimes able to detect a circle, a triangle, the letter *E* and the number *4* when drawn on the skin. In other areas on his left side he did not even attempt to guess at the applied stimulus.

As already noted for pain, all sensations showed a notably reduced adaptation time. Duration of after-sensation was also diminished. In several instances, the pain sense revealed fluctuation phenomena, in spots there being two or three variations between the pain and the pressure sensation.

Sensory Extinction Phenomenon.—Simultaneous application of painful stimuli to corresponding foci on the two sides of the body produced (*a*) reduction in adaptation time, (*b*) a sharp rise in the sensory threshold, so that he felt no pain at all or just a dull sense of pressure, or (*c*) total extinction of the perception on the left side of the body. When the stimuli were applied separately, he was able to appreciate a sharp point on each side of the trunk. With "double stimulation" he often was unaware that anything was touching him on the left side, unless the stimulus on the right side was removed within the sensory adaptation time for the left side. When the stimuli were unequal—for instance, 25 Gm. on the left side and 10 Gm. on the right—dulling of sensation still occurred on the left side. When the stimulus was stronger on the right side, the phenomenon was even more apparent, sensation on the left side becoming totally extinct.

The phenomenon could also be produced with simultaneous applications of mixed stimuli. The extinction phenomenon for the tactile sense on the left side could always be elicited by a simultaneous painful stimulus on the right side. The same was true when conditions were reversed; i. e., with a tactile stimulus on the

6. Psychologically, all sensations show the phenomenon of negative adaptation. Under continual and unchanging application of a given stimulus, the characteristic sensation evoked disappears after a given interval. This interval is termed "the sensory adaptation time" in this paper and should not be confused with the word "adaptation" as used in the physiologic sense by Adrian and others.

right side, the pain sense was inhibited or obliterated on the left side. The vibration sense was not inhibited on the left side with double stimulation; painful, tactile or other forms of stimuli applied to the right side did not obliterate the vibratory stimulus applied simultaneously to the left side. However, vibratory stimuli on the right side did inhibit painful and tactile stimuli on the left side.[7]

Tactile perception of movement, such as rubbing or scratching, along the skin of the left hand was preserved. But when both the right and the left hand were rubbed simultaneously, the patient felt the movement only on the right hand. As soon as the stimulus was withdrawn from the right side, he felt the rubbing or scratching on the left side. Again, when the rubbing on the right side was resumed, the sensation due to the scratch stimulus on the left side disappeared. This could be demonstrated in repeated tests, probably because in stimulation by rubbing or scratching the adaptation time does not seem to be a factor. Graphesthesia, perception of the direction of drawn lines and point localization in areas on the left side, such as over the trunk, were inhibited by a painful stimulus on the right. The extinction of such perceptions, which involve spatial and temporal elements, was much more conspicuous than that of any of the simple modalities, such as painful tactile and thermal sensations.

Mentally, the patient was well oriented and clear. He made no errors in response to stimulations on the right side of his body. Here, graphesthetic perception and the simple modalities were not impaired when the left side was stimulated simultaneously. Mental distraction, such as engaging the patient in conversation, did not significantly alter the sensory responses to stimuli applied either to his left or to his right side. In contrast to this, however, when the patient was requested to concentrate on sensation on his left side during the double stimulation, he perceived only sensation on the right side. Special psychologic tests showed that the reaction time was normal and comprehension of instructions good. Performances in the vocabulary and information tests indicated a pretraumatic average intellectual level. This finding was in harmony with the educational history of two years of high school. Retentive capacity was found to be relatively defective, at borderline level, and a slightly poorer than average reasoning ability was shown. The conclusion was that moderate impairment in intellectual efficiency had followed the accident.

CASE 2.—J. S., a Marine sergeant aged 28, was shot in the right side of the head while in battle. The bullet went through his helmet, striking the right parietal bone. He did not lose consciousness, but immediately after he was hit he felt his left hand become "dead." This condition lasted a week. A craniotomy was performed at a base hospital, where fragments of bone in the right parietal region were removed and the underlying cortex was found contused. The patient's condition improved. One month after the injury, he complained that the left hand felt "half asleep."

Physical examination revealed a pulsating wound, with a drain, in the right midparietal region.

Neurologic examination at that time showed complete astereognosis in the left hand and on the left side of the mouth, where he was unable to recognize a cigaret or a spoon held between the lips. Other sensory defects in the left hand were impairment of sense of position and recognition of initiation of movement in the fingers, defective two point discrimination and point localization, impairment of superficial and fine tactile sense and inability to judge weights. Pain and temperature senses appeared to be uninvolved when each side of the body or the extremities on the two sides were tested separately. In time the patient improved physically, and finally the drain was removed.

Four months after the injury, the neurologic status was practically the same as already noted, but the following additional changes were found: 1. Reduction of the sensory adaptation time. Although the pain sense seemed equal on the two sides when they were tested separately, the adaptation time for pain sense was reduced over the entire left side of the body, especially the hand. Three to five seconds after its application, the prick of a needle point became dull, changing to a pressure sensation, which, in turn, disappeared within seven to nine seconds. On the right side, the pain lingered for thirty-five to sixty-five seconds after the application of the stimulus. 2. Dulling or extinction of pain in the affected area as tested with the double stimulation method. Pain sense was found to be much reduced or obliterated on the left side during simultaneous, or double, stimulation. Moreover, although the patient clearly felt the prick of a pin in the left hand, this sensation was rapidly diminished or dulled when the right hand was stimulated simultaneously. In the various areas tested with the method of double stimulation, the dulling or extinction of cutaneous pain sensibility manifested itself on the left side of the body by the following phenomena: (*a*) further reduction in the adaptation time, so that one or two seconds after the application of the double stimulus the pain was replaced by pressure sensation and within three to five seconds the pressure sensation disappeared (compare with the effect of a single stimulus applied to the left side, as previously noted); (*b*) rise in the sensory threshold, so that the painful stimulus did not seem sharp, resulting in a sensation of pressure on the left side and in a sense of pain on the right side during double painful stimulation, or (*c*) total extinction of the sensation, so that the patient did not appreciate even the pressure of the applied stimulus of 25 Gm. with the needle point or realize that he was being touched at all on the left side. The type of inhibitory response on the left side seemed to vary in different parts of the body but was most pronounced in the left hand, especially when the stimulus on the right side was much stronger than that on the left.

An even more striking example of the dulling or extinction phenomenon was found in testing his tactile perception of letters, numbers or geometric figures drawn with a pencil on the skin (graphesthesia). A triangle, a circle, the letter *E* or the number *4* was well perceived when drawn individually on any part of the right or the left side of his body. However, when the left side was thus tested while the corresponding area on the right side was simultaneously pricked with a pin or gently rubbed or tickled with a pencil point, the patient was unable to detect the images drawn on the left side. Point localization was similarly influenced under the conditions of double stimulation. There was no difficulty in the graphesthetic perception or in point localization on the right side with the double stimulation method. The extinction phenomenon was much more conspicuous for graphesthesia than for sensations of pain, touch or temperature. Mixing or varying the stimuli did not materially interfere with the elicitation of the phenomenon.

Five months after the injury, the patient complained that when his left hand was out of sight he was unaware

7. It must be borne in mind that in testing for the vibration sense, tactile sensitivity is also being stimulated. It is possible, then, that the contact or weight, and not the vibration, of a tuning fork applied to the right wrist is responsible for the inhibition of painful or other stimuli applied simultaneously to the corresponding area on the left wrist.

of its presence and that he did not know its location. Occasionally, when his left hand dropped, he did not realize that it had done so. The position sense was slightly impaired in the fingers but in no other joints. The neurologic status remained unchanged. He continued to show the extinction and allied phenomena on his left side during double sensory stimulation. Adaptation time was notably reduced, and after-sensation was shortened or lost on the left side. Thus, he felt the sting or the tingling of a pinprick on the right side three seconds after the withdrawal of the stimulus, whereas there was momentary or no "after-sting" on the left side. Astereognosis in the left hand was still present. Despite the astereognosis, graphesthetic perception in the left hand was normal when tested for separately but was lost completely during double stimulation.

Other patients with lesions of the parietal cortex exhibited various stages and degrees of the sensory dulling or extinction phenomenon with the double stimulation method. In some patients there was only further reduction in the sensory adaptation time; in others there was transient dulling or raising of the sensory threshold, and in still others there was complete extinction of sensation, on the affected side. Most striking was the unilateral obscuration or abolition of graphesthetic perception with the double stimulation method. This was found in patients in whom no extinction phenomenon could be demonstrated for the simple modalities. Another conspicuous finding was that of obliteration of perception of a rubbing or scratching movement of a digit on the affected side during simultaneous stimulation on the two sides of the body.

The extinction phenomenon was best elicited when the stimuli were applied to corresponding points on the two sides of the body, such as the hands or the feet; but this, or the dulling of sensation, could be produced as well when the stimuli were applied to different parts of the body, e. g., the hand on one side and the foot on the other. The phenomenon was also manifest, but to a lesser extent, when the stimuli were applied at two points, such as the neck and the hand, on the affected side. In a few patients with hemiplegia, examination with the double stimulation method failed to disclose any dulling or extinction of sensation. These patients did not have demonstrable sensory defects. Evidently, not every one with a cerebral lesion exhibits the phenomenon.

LESIONS OF THE SPINAL CORD

In a series of patients with injuries of the spinal cord who had the Brown-Séquard syndrome, there were a few in whom the sensory extinction phenomenon could be clearly demonstrated. The following case is an example.

CASE 3.—W. H. L., a 26 year old Marine corporal, sustained a gunshot wound in the neck while in combat in the South Pacific. He did not realize that he was injured until he found himself on the ground, with the delusion that his legs were disconnected from his body and hanging up in the air. For ten minutes he felt as though the legs were not his own. Finally, he realized that he was paralyzed and "numb" below the shoulders.

Examination revealed a small gunshot wound in the neck. The neck was swollen and discolored with blood. A roentgenogram showed a comminuted fracture of the laminas of the seventh cervical and first thoracic vertebrae on the right side. Neurologically, there was total loss of motor power and sensation below the sixth cervical dermatome bilaterally. One month after the injury, there was some restitution of function of the spinal cord. Motor power in the upper extremities and in the left foot began to return. Two months after the injury, the improvement was more apparent, and he showed signs of a lesion on the right side of the spinal cord with a Brown-Séquard syndrome.

Five months after the injury, he began to walk. Neurologic examination showed spastic weakness in both lower extremities, especially on the right side, and defective sensation on the left side below the seventh cervical dermatome, with the greatest involvement in the lumbar distribution. Deep pressure sense, point localization and graphesthetic perception were preserved throughout. Two point discrimination was much reduced on the left side. Although, with the ordinary method of sensory examination there was no apparent defect of pain sense on the right side of the body, the sensory adaptation times for pain and pressure sensation were decreased below the level of the seventh cervical dermatome. This reduction of adaptation time was the only clue to residual sensory defect in the formerly anesthetic area.

Sensory Extinction Phenomena with Double Stimulation Method.—On one examination the patient showed dulling of the pain sense in the left thigh and over the left side of the trunk. When asked what he felt, he stated, "It seems as if I don't pay attention to my left side when both sides are being stimulated." Subsequent examinations disclosed various areas of dulling of sensation on the left side. In the sacral dermatomes there were zones in which the cutaneous sensory extinction phenomenon for pain was present. Double stimulation over the buttocks with a needle point, using a 10 Gm. weight on the left side and a 25 Gm. weight on the right side, yielded sensation only on the right side, even though the patient attempted to concentrate on his left side. He was able to appreciate the pain and pressure of the point during single stimlulation on the left side. On this side, the adaptation time for pain sensation with a 10 Gm. stimulus was five seconds, and that for pressure sensation, seventeen seconds. The painful sensation on the left buttock was dulled or abolished as soon as a stimulus was applied to the right buttock. The pain and pressure sensations in the left sacral dermatomes were also inhibited by a simultaneous stimulus applied to the right side of the neck and to a lesser extent, by one applied to the left side, as over the face or the upper part of the trunk. Interesting was the absence in the affected area of obscuration or extinction of graphesthesia, a phenomenon which is often associated with cerebral lesions. Other related phenomena noted on the left side during double stimulation were reduction of sensory adaptation time and raising of the sensory threshold. These were inconstant, but were significantly present on repeated occasions in the defective sensory areas.

This case is an example of cutaneous sensory extinction in a patient with a lesion of the spinal

cord and demonstrates that the phenomenon is not necessarily due to cerebral damage. In general, most of the patients in the series with lesions of the spinal cord did not manifest total extinction of sensation. A few showed transient and further reduction of the sensory adaptation time. Others manifested a rise in the sensory threshold in the affected area. Again, attention was evidently not a factor, for the patient was instructed, and he sincerely attempted, to concentrate on the side on which sensation was to be inhibited.

LESIONS OF THE SPINAL ROOTS AND PERIPHERAL NERVES

Several patients with gunshot wounds of the cauda equina or the cervical roots were examined. The sensory defects found were of all degrees and often involved all modalities. Besides the sensory disturbances commonly noted, there were reduction of sensory adaptation time, decreased after-sensation and impairment of two point discrimination. Graphesthesia was not disturbed unless sensation was defective to such an extent that the patient was unable to detect even deep pressure. No extinction phenomena were elicited with the double stimulation method. In 2 patients with lesions of the cauda equina there appeared to be a further reduction in the sensory adaptation time in the affected area. This was the only evidence or suggestion of a form of sensory extinction in these patients. None of the patients with lesions of peripheral nerves showed any of the complete extinction phenomena. However, there were several patients with causalgia who demonstrated what seemed to be a corollary to the extinction phenomenon, namely, accentuation or intensification of the pain sense. Stimulation in the healthy areas precipitated or aggravated spontaneous pain in the causalgic, or painful, limb. A similar phenomenon has been observed in the opposite, normal limb, that is, perception of pain in the normal limb when the opposite affected limb was stimulated. This has been termed synesthesialgia by Wechsler.[8] It is related to allocheiria, in which the patient refers the tactile stimulus to a corresponding spot on the opposite limb. Wechsler stated that in some patients with "cerebral lesions, possibly also in cord disease and in hysteria," this type of sensory referral may be observed. The following cases are examples.

CASE 4.—D. H. C., a 28 year old Marine sergeant, was shot in the left arm. The arm jerked behind him, with the elbow bent, the wrist flexed sharply and the fingers contracted into his palm. There was no pain, and he thought for several moments that his arm had been shot off. There was brisk arterial bleeding. Sensation was lost below the wound, and the left upper extremity was paralyzed from the shoulder down. He was given emergency treatment. For three weeks, the motor and sensory defects remained unchanged except for a mild burning sensation in the skin across the metacarpal bones. One month after the injury, the median and ulnar nerves were explored for several inches and were found to be apparently intact. No lesion was noted except at a point where the brachial artery was constricted, apparently due to scarring. After this operation, there developed severe burning pain in the palm. The pain was worse with exposure to cold and was partially relieved by moistening the affected hand. The patient formed the habit of going to the water fountain every half-hour to wet both hands.

Phenomenon of Intensification of Pain.—The patient found relief from the spontaneous pain in the left hand when he wet the right hand. A drying or rubbing movement in the palm of the right hand produced a sharp exacerbation of the burning pain in the left palm. Thus, if he held a cup or if he gripped any other object with his right hand and this object happened to slip, or if the right hand moved across an object, an excruciating pain appeared in the left palm. A deep tickling of the ball of either foot also produced pain in the affected hand. However, application of a rubbing stimulus to other areas, such as the dorsum of the hand or the back of the neck, had no influence on the pain in the left hand. The patient also noted that emotional stress or the sound of a scraping noise, such as shuffling feet, or even the sight of a scratching movement evoked burning and sharp pain in the left palm. The most sensitive trigger point, however, was the middle of the right, or normal, palm. The patient had the symptoms of a typical major causalgia, with prominent vasomotor, sudomotor and trophic changes. The radial pulse was weak. There was marked hyperesthesia in the sensory distribution of the median and ulnar nerves. Pressure on the brachial artery brought relief of the spontaneous pain. Three months after the injury, the left median and ulnar nerves were surgically explored. Both nerves were found to be encased with scar tissue. The brachial artery was so scarred that it could not be identified. Some of the vessel strands were severed, and neurolysis of the scarred nerves was performed.

This operation was followed by notable relief of pain. Stimulation of the right side no longer influenced sensation over the left side. Trophic changes diminished. However, there were residual sensory defects in the distribution of the median, ulnar and medial antebrachial cutaneous nerves. There was still reduction of two point discrimination. The adaptation time for clear appreciation of a point was reduced. There was definite hyperpathia; the pinprick, although dull, seemed much more painful and spread over a greater area on the affected side than on the normal one. After-sensation was increased on the left side. There was no agraphesthesia and no sensory extinction phenomenon with the double method of stimulation. Graphesthetic perception was impaired in the left palm when the figure was drawn too rapidly. With slow drawing, the unpleasantness and spread of sensation produced by the stimulating object were not too great to interfere with the correct perception of the stimulus, so that the patient could recognize the figure written in

8. Wechsler, I. S.: Textbook of Clinical Neurology, Philadelphia, W. B. Saunders Company, 1943, p. 44.

his affected hand. After the last operation, the pain in the left palm was only occasionally intensified by a sudden scratching or scraping noise or by pronounced rubbing in the right palm. Scratching of the soles was no longer provocative.

Intramuscular injection of histamine acid phosphate, 2 mg., caused generalized redness and flushing of the face. With this injection there was excruciating pain in the left palm, which lasted twenty minutes. The pain due to injection of histamine was relieved by immersing the hand in cold water. Intramuscular injection of nicotinic acid, 30 mg., also produced a generalized flush, which spread from the head downward. The skin throughout the body felt hot and stinging, but there was no precipitation of pain in the left palm, as was found with histamine.

There were other patients with causalgia of the hand who showed this remarkable phenomenon, namely, accentuation of burning pain by application of a scraping stimulus to distant parts of the body, especially in the midportion of the opposite palm. In some patients the dry rubbing of any part of the body produced pain in the palm. In others the thought, sight or noise of a scratching, rubbing or scraping motion evoked severe tingling in the affected hand. There were also patients who had causalgia in the foot due to injury to the sciatic or the tibial nerve. In some of these unfortunate persons movement or scratching of the sole of the healthy foot increased the pain in the causalgic foot. The following case is an example.

CASE 5.—E. C. O., a 21 year old Marine sergeant, sustained shrapnel wounds in the right lower extremity, the left foot and the right eye. The right femur was fractured, and he had signs of a complete lesion of the right sciatic nerve. He was given appropriate treatment. Two days after the injury, a burning, sticking pain appeared in the right foot, especially in the toes. The right lower extremity was immobilized, but the pain in the toes persisted. Despite the lack of cutaneous sensation in this extremity, he had a "bursting" and "exploding" pain in the ankle, foot and toes. Five months later, he happened to run his hand over a scar on the lateral aspect of the right thigh. This produced severe tingling and burning in all the toes of the right foot. The sensation seemed to be limited to the plantar aspect of the toes. Later, he also noted that mild pressure on a scar situated in the right popliteal space produced tingling in all the toes of the right foot. Further studies showed that deep pressure, deep pain or a scratching movement over the plantar surface of the arch of the left foot evoked intense tingling and sharp, burning pain in all the toes of the right foot. The midportion of the plantar surface of the left, or normal, foot was the most sensitive area for the production of contralateral symptoms. Firm bending of all or of one toe on the left foot produced tingling and burning only in the right great toe. Rubbing or any other form of stimulation on the dorsum of the left foot, of the palms or any other part of the body except the trigger points previously described did not yield distant accentuation of burning in the right foot or toes. In fact, even rubbing or stimulation of the affected right foot was without effect. As already noted, there was complete loss of sensory and motor function of the right sciatic nerve. The right foot was dry, and electrical cutaneous resistance, as measured by the "neurodermometer," was very high, indicating sympathetic paralysis in the right foot and part of the leg (distribution of the sciatic nerve).

Emotionally, the patient was tense, irritable and hostile. He was puzzled by the fact that during his confinement to the hospital he had great urges for action and a desire to kill and to be exposed to danger. This aggression was expressed in dreams. The patient said that: "Occasionally, I have queer dreams in which my natural emotions seem to be suppressed. For example, I am in a pill box and am firing at the occupants, being frustrated in my attempts to kill them by such things as my rifle, which seemingly falls apart, or fails to function in some vital part. At the climax, I usually awaken, sometimes perspiring and breathing heavily, and with a great deal of pain in my foot."

The patient claimed that this was the only evidence of relationship between pain in the foot and emotional stress. Despite his tendency to suppress or inhibit his anger or anxiety, there was no accentuation or precipitation of the intense bursting or exploding variety of pain in his toes and foot, as evoked by stimulation of the trigger points. On one occasion the patient was so uncomfortable that he expressed a desire to have his right leg amputated, "since it was no good anyway."

This case illustrates that sensory stimulation in one area may intensify or precipitate spontaneous pain in the corresponding area on the opposite side of the body. The presence of severe burning pain in a foot which has no sensory, motor or sympathetic nerve supply is suggestive of phantom limb. Sometimes phantom limb may occur, without amputation, in cases of severe injury to the peripheral nerves in which there is loss of sensation in distal parts of the affected extremity.[9]

COMMENT

The foregoing case reports are illustrative of a fairly large group.[10] From these observations, it is evident that sensation may be made extinct or pain may be intensified on one part of the body by a stimulus applied to another part of the body.

In the first group of cases, that of cutaneous sensory extinction, the phenomenon was demonstrable in an area deficient in sensation when this and a normal area of the skin were stimulated simultaneously. The phenomenon is most often encountered in cases of cerebral lesions, infrequently in cases of disease of the spinal cord and, except for slight dulling of sensation, practically never in cases of peripheral nerve defects. The sensory extinction phenomenon may manifest itself in varying degrees, from a slight reduction in sensory adaptation time, or rise in the

9. Riddoch, G.: Phantom Limbs and Body Shape, Brain **64**:197-222, 1941.

10. Because of military regulations, detailed statistics cannot be presented at this time.

sensory threshold, with dulling of the pain sense, to complete extinction of sensibility. The sensibility which seems to be most vulnerable and becomes readily extinct on the affected side during double, or simultaneous, stimulation is graphesthesia, a perceptual process which requires temporal and spatial sensory integration at the cortical level. The least vulnerable has been found to be the sense of vibration, which is known to be appreciated at the thalamic, and not at the cortical, sensory level.[11] On the basis of these observations, it would seem that the sensory extinction and allied phenomena take place in the cerebral cortex and are particularly evident when one cortex is diseased. However, since the phenomena have been elicited in patients with lesions at lower levels of the nervous system, it is obvious that they are not entirely dependent on the structural condition of the sensory cortex.

There must be physiologic, rather than anatomic, elements to account for the fact that tactual stimulation of one area influences (inhibits) the corresponding area on the other side of the body. A physiologic or psychologic mechanism which is known to operate in the normal subject is rivalry between the sensations arising from the two sides or different parts of the body. Heyman's law states that simultaneous stimuli inhibit each other.[12] Naturally, if there is a difference between the perception of the two applied stimuli, the stronger sensation will have a more powerful inhibitory effect on the weaker than will the latter on the former. Sensations between the two sides are in constant competition with each other, and, as noted in the pathologic states described in the first 3 case reports, the stronger the sensation is on one side, the less the patient perceives on the weak side.

The principle of sensory dominance can be demonstrated to a certain extent in the normal subject, as when a strong painful stimulus at one point inhibits pain at another. The relief of pain obtained with the method of counter-irritation is based on this principle. But why sensory extinction is so apparent in persons with cerebral lesions and less evident in those with lesions at lower levels or in the normal subject is difficult to explain. The factor of "attention" does not seem to play an important role, for, as has repeatedly been described in the case reports, the focusing of the patient's attention on the affected side did not appreciably influence the extinction or obscuration phenomenon. Occasionally, the patient complained that the stronger sensation distracted him from his ability to perceive sensation on the opposite side, but this evidently was not due to inattention, for the patient concentrated on the stimulus applied to the affected side.[13]

A theory which may account for the occurrence of the phenomenon in patients with cerebral lesions is that of Goldstein,[14] to the effect that the available nerve energy, which is constant, is utilized better and to a greater extent by the normal cortex, so that an insufficient quantity is left for the use of the diseased cortex in effecting a performance. Still, this hypothesis does not explain why some patients with sensory cortical lesions do and others do not show the extinction or the allied phenomena, and why some patients with lesions in the spinal cord manifest the phenomenon. Emotional factors, such as suggestion or hysterical reactions, are possibilities to be considered. In fact, in a patient with a hysterical hemisensory syndrome, the phenomenon of extinction of a dull sensation was elicited. This, however, was inconstant, and the sensory distribution which he manifested had no known anatomic pattern.

Interesting and significant is the prominence of the extinction or dulling of sensation when simultaneous stimulations are made in corresponding areas on the two sides of the body, such as the two hands, arms, thighs, legs or clavicular regions. The sensory phenomena are not so apparent when the arm on one side and the trunk or the leg on the other or on the same side are stimulated simultaneously. In a patient with a lesion of the spinal cord, simultaneous stimulation of two different areas on the same side produced some inhibition in the hypalgesic zone, thus suggesting that the inhibition may be ipsilateral. Although the phenomenon could be elicited by application of two stimuli to any part of the body, the best cutaneous sensory extinction can be demonstrated when two corresponding points, on opposite sides of the body, are stimulated simultaneously.

11. Weinstein, E. A., and Bender, M. B.: Dissociation of Deep Sensibility at Different Levels of the Central Nervous System, Arch. Neurol. & Psychiat. **43**:488 (March) 1940.

12. Cited by Guilford, J. P.: Fluctuation of Attention with Weak Visual Stimuli, Am. J. Psychol. **38**:534, 1926.

13. It is well known that distraction, attitude and suggestion may modify the threshold and the manner of reaction to pain (Hardy, J. D.; Wolff, H. G., and Goodell, H.: The Pain Threshold in Man, A. Research Nerv. & Ment. Dis., Proc. [1942] **23**:1, 1943), but how and where these modifications take place is not clearly understood.

14. Goldstein, K., in discussion on Bender and Furlow,[3] and personal communications to the author.

In the second group of cases, spontaneous pain could be precipitated or aggravated by scratching or dry rubbing in another part of the body. The topographic factor seemed also to be prominent in this group. In case 4, it was the cutaneous stimuli coming, chiefly, from the right, or normal, palm, such as dry rubbing or scratching, which influenced sensation (precipitation of spontaneous pain) in the opposite, or causalgic, palm. In case 5, deep pressure, rubbing or painful stimuli in the left, or normal, foot caused pain and burning in the causalgic toes on the right side.

The phenomena of contralateral sensory extinction or dulling, contralateral intensification of pain, synesthesialgia and allocheiria all show the functional and topographic relationship between the sensations on the two sides of the body. At what level in the nervous system this relationship, inhibition of a painful stimulus or precipitation of pain, occurs is difficult to ascertain. It may be in the spinal cord, the thalamus or the cortex, but perhaps largely in the cortex. Livingston,[15] in his monograph on pain mechanism, stated that he had personally observed some 35 cases in which a long-established pain syndrome in one limb spread to involve the contralateral limb in the same distribution. This he called the "mirror image phenomenon." He also cited Weir Mitchell as having frequently made similar observations. Mitchell[16] described a case in which dry rubbing on or use of the normal palm caused pain in the causalgic palm. As an explanation of the spread of pain to the opposite, or even to the same, side of the body, Livingston[15] stated that some "dynamic process has been initiated within the spinal cord that may persist after the original stimulus is withdrawn," and "that the original initiative lesion initiates some changes in the activities of the regulatory centers of the central nervous system that eventually acquires a self-sustaining momentum." In other words, the induction of sensory disturbances on the side opposite the original cutaneous focus is due to some physiologic, or perhaps psychologic, change in the central regulating or integrating levels of sensation. Of course, this is pure speculation, but there must be some sort of sensitization in the cortex or the thalamus to explain the increase in pain.[17]

These clinical observations recall the experiments of Dusser de Barenne[2] in which painting a few square millimeters of the cortical arm area on one side with strychnine produced hyperalgesia in both arms in the monkey. These experiments with strychnine suggest that the precipitation of pain in the distribution of a very sensitive nerve on stimulating the corresponding cutaneous area of the opposite hand or foot in man is due to some change in the cortex, which has been sensitized by a psychic or physiologic agent or through some other mechanism. Why in some subjects a rubbing or scratching motion is the only type of stimulus which accentuates pain on the opposite side is not clearly understood, unless a moving stimulus is more effective than a static tactile or thermal stimulus, to which the organism readily adapts. In some cases, deep pressure and painful stimuli, especially when applied repeatedly, precipitate burning or boring pain in the affected hand or foot. In others, even the sight, hearing or thought of a scratching movement will produce pain, thus indicating that the reflex response to pain goes through a cerebral or cortical arc. There is also a possibility that this reflex response of pain in the affected palm or foot on stimulation of the normal area occurs at a spinal level by way of the pain fibers which are transmitted by the vascular tree.[18] Thus, a scratching or scraping movement produces a generalized vasomotor response, which is bound to include the vessels in the affected extremity. In turn, the vasomotor reaction in a hypersensitive area may precipitate a severe burning or tingling pain by stimulating the sensitized pain fibers in the blood vessels.

When all the facts are compiled, it appears that the unilateral sensory extinction phenomenon with the method of double stimulation and the precipitation of contralateral causalgic pain with a unilateral rubbing or scratching stimulus are closely related and are, respectively, the inhibitory and the excitatory phase of the same phenomenon. The physiologic or psychologic interaction of these phases most probably occurs in the cerebral cortex, although it may also

15. Livingston, W. K.: Pain Mechanisms, New York, The Macmillan Company, 1943.

16. Mitchell, S. W.: Injuries of Nerves and Their Consequences, Philadelphia, J. B. Lippincott & Company, 1872.

17. A similar mechanism has been postulated in the mysterious syndrome of phantom limb. The sensation of the phantom limb has been attributed by some authors to sensitization in the parietal cortex, with a "cortical engraving." Based on this theory de Gutiérrez-Mahoney (de Gutiérrez-Mahoney, C. G.: The Treatment of Painful Phantom Limb by Removal of Post-Central Cortex, J. Neurosurg. **1**:156 [March] 1944) excised the parietal cortex and thus successfully abolished the painful "phantom limb" on the opposite side.

18. Foerster, O.; Altenburger, H., and Kroll, F. W.: Ueber die Beziehungen des vegetativen Nervensystems zur Sensibilität, Ztschr. f. d. ges. Neurol. u. Psychiat. **121**:139, 1929.

take place at lower integrating sensory levels. In either case, whether there is inhibition or excitation of pain, these observations reveal a bilateral functional relationship of the cortex to sensation on the two sides of the body and lend support to Dusser de Barenne's conclusions drawn from animal experiments, that each sensory cortex may influence sensation on both sides of the body.

SUMMARY AND CONCLUSIONS

In the cases described, dulling or extinction of cutaneous sensation occurred in an affected area, when this and a normal area, usually the corresponding one on the opposite side of the body, were stimulated simultaneously. When the affected area alone was stimulated, it might be fairly sentient. In other cases, pain was precipitated or spontaneous pain aggravated in a causalgic limb when the opposite hand or foot or some distant part of the body was stimulated.

The cutaneous sensory extinction and the precipitation of pain by stimuli from the opposite side of the body are probably related, one being the positive and the other the negative phase of the same phenomenon. It is hypothesized that both phases of the phenomenon take place in the sensory cortex and that there is a bilateral functional relationship between the sensations of the two sides of the body.

MAN'S FRONTAL LOBES

A CRITICAL REVIEW

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Examination of the current literature concerning the frontal lobes reveals an almost universal belief that surgical removals from this area must produce serious psychologic defects. The evidence on which the belief is founded, however, is not nearly so satisfactory as one might suppose. In this paper I propose to review and evaluate the published reports which attempt to analyze the functions of the frontal lobes on the basis of neurosurgical material. In the review, emphasis is laid on problems of method which are common to any such analysis, whatever region of the brain may be concerned.

The occasion for a reevaluation of theories concerned with the frontal lobes was a fortunate opportunity to observe the social adjustment of K. M., a patient of Dr. Wilder Penfield's, six years after a partial bilateral frontal lobectomy (Hebb and Penfield,[1] 1940). The patient's excellent recovery showed that a large bilateral removal is not always followed by gross defects of behavior. The differences between this case and others, in which serious maladjustments have been found, demanded explanation. What factors determine whether the outcome of operation will be good or bad? The answer to this question is as important for therapy as for psychologic theory. Accordingly, although the present discussion deals throughout with the theoretic problem of localization of function, its conclusions also have a practical significance for the clinician.

PERSONAL ADJUSTMENT SIX YEARS AFTER BILATERAL "LOBECTOMY"

The preceding report on K. M. (Hebb and Penfield[1]) was written a year after operation. At the age of 16 years a fracture in the frontal area destroyed both frontal poles of the brain. For ten years increasingly severe epileptic attacks made the patient an irresponsible charge to his parents. Between outright convulsions he was childish, violent, stubborn and destructive, with gross defects of memory and ordinary judgment. There were periods when he was normally responsive and restrained, but he was not himself aware of the transition to one of his violent and stubborn moods. Others could detect it only by the actual change of behavior. He would go outdoors in the winter weather of Nova Scotia without warm clothing, for example; and as to persuading him to act differently, "you might as well talk to a post." He might set out for the grocer's or to mail a letter, and return late at night without having completed his errand. He might walk into any house he saw and destroy anything in his way. Since he was strong and big, the neighbors were terrified of him, and even when he was not in one of his violent moods he sometimes took a malicious pleasure in pretending that he was, in order to frighten others.

Now, six years after operation, his relatives are still sure, as they were a year after the lobectomy, that he has become normal in every way. The independent testimony of three residents of the village—taxi driver, storekeeper and waitress—is that there is nothing wrong with K. M.'s behavior now and that he is one of the most popular persons in the village. The malicious joking has stopped with the improvement in other behavior.

In February 1942 he joined the Canadian army. This was at a time when Canadian headquarters in England had been sending home psychoneurotic men and misfits for a year or more. Every commanding officer in Canada was under pressure to find and weed out unsatisfactory personnel, and efforts were made to detect such men early in training. Recruits at that time did not have psychiatric examination as a routine, but there was a directorate of personnel selection, staffed mainly with psychologists, to deal with misfits. This mechanism for handling the maladjusted or mentally incompetent as they were discovered in training was freely used.

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1. Hebb, D. O., and Penfield, W.: Human Behavior After Extensive Bilateral Removal from the Frontal Lobes, Arch. Neurol. & Psychiat. **44**:421-438 (Aug.) 1940.

Nevertheless, K. M. was in the army for ten months, and had been sent overseas, before an epileptic attack, precipitated by hard labor, brought him to the medical officer's attention, when he was discharged.

He had apparently had no other attacks since his first postoperative year (when he twice stopped taking phenobarbital, 1 grain [0.065 Gm.] a day, and each time had an attack). Since the attack in England he has had three other seizures in a year and a half. According to the patient, these occurred in spite of his taking the phenobarbital as usual. The recent convulsions have always been at night, during sleep. He has also on perhaps five or six occasions had a slight and transient state of confusion as he was about to fall asleep.

K. M. has no trade or special skill, but in a wartime shortage of labor he has no trouble in finding jobs, which he does himself, without any family guidance. He has in fact had half a dozen jobs since his discharge from the army. He works in a neighboring town (population about 4,000), where he is not especially known. He is liked by his employers, as far as can be ascertained, and apparently other employers entice him away with offers of better working conditions, and so on. When his family was first interviewed, with the object of arranging a later interview with K. M. himself, he had just given two weeks' notice to his employer. He worked those two weeks as usual and then quit for what were undoubtedly better working conditions. It seemed, however, that his brother was not pleased with the frequent changes, and in conversation K. M. showed no great concern about finding a job with permanence or future. He apparently saved enough from each week's pay so that he always had money when he needed it; but nothing more could be discovered about his spending habits, and he probably is making no effort to save for the future. However, his good social relationships and his provision for at least a few days ahead show no sign of the "lack of foresight" by which Freeman and Watts [2] interpret their patients' social errors. The amount of foresight needed to avoid the tactlessness described by Freeman and Watts is at most of the order of minutes; K. M.'s foresight certainly anticipates his own actions days or weeks in the future, and possibly to more remote periods. While the examiner was trying to find out whether K. M. was making any effort to "better" himself, the latter mentioned a half-formed intention of going to Toronto, about 1,000 miles (1,600 kilometers) away. This confirms the impression that K. M. was rather too ready to shift jobs, since he had no prospects of a particular kind of work when he got to Toronto, but it also suggests an unexpected degree of initiative.

The patient was tested with Goldstein's [3] figures, to be copied with match sticks from memory, and with single and double alternation and delayed response problems. No suggestion of defect was discovered, a result which perhaps might have been predicted from the patient's earlier performance on a varied battery of other tests (Hebb and Penfield [1]).

The conditions of testing delayed response were crude and did not duplicate those of Jacobsen [4] or Malmo.[5] However, these authors generalized their results, reasonably enough, beyond the actual laboratory conditions in which they were obtained, and it may be said that the human patient with bilateral loss of the frontal association areas is capable of a kind of performance which the lower primates with similar lesions cannot carry out.

There is no reason to treat such a result as puzzling or improbable. Even if the frontal lobe in man has the same functions as that in the lower primates, the human brain as a whole is certainly more developed and may be capable of solving delayed response problems by more than one mechanism. The capacity for speech in itself provides a mode of solution which the monkey does not have. Supposing, then, that the human frontal lobe contains a mechanism of delayed response, the speech area and the rest of the brain may provide another. If so, one would find no evident loss of delayed response in a man with the same injury to the frontal lobe which prevents delayed response in monkeys.

EXPLANATION OF DISCREPANCY BETWEEN K. M.'S CASE AND OTHER CLINICAL CASES

K. M.'s lack of gross defect is unexpected, to say the least. Other cases of large bilateral surgical destruction of frontal areas have been

2. Freeman, W., and Watts, J. W.: Psychosurgery: Intelligence, Emotion and Social Behavior Following Prefrontal Lobotomy for Mental Disorders, Springfield, Ill., Charles C Thomas, Publisher, 1942.

3. Goldstein, K., and Katz, S. E.: The Psychopathology of Pick's Disease, Arch. Neurol. & Psychiat. **38**:473-490 (Sept.) 1937.

4. Jacobsen, C. F.: Studies of Cerebral Functions in Primates: I. The Functions of the Frontal Association Areas in Monkeys, Comparative Psychology Monographs, Baltimore, Johns Hopkins Press, 1936, vol. 13, no. 3, pp. 3-60.

5. Malmo, R. B.: Interference Factors in Delayed Response in Monkeys After Removal of Frontal Lobes, J. Neurophysiol. **5**:295-308, 1942.

reported, particularly by Brickner,[6] Nichols and Hunt[7] and Mixter, Tillotson and Wies.[8] All 3 patients in these reports have had to have continued care and detention, and it is assumed, by some of these authors and by others, that the reason for the social incapacity is to be found in the surgical loss of frontal lobe tissue.

The patient operated on by Dr. Penfield presents an entirely different picture. No psychologic defects can be definitely demonstrated. He is, indeed, a strikingly easy-going, carefree fellow, and his lack of concern for the distant future could be due to the cerebral excision. But to prove that this is so is another matter. One can find plenty of normal persons with no more care for the morrow, and certainly with less concern about giving their employers notice when they are going to change jobs. Among patients who have recovered from long hospitalization for tuberculosis there is not infrequently the same easy feeling that tomorrow must be left to care for itself. It is hard in this case to evaluate the psychologic effect of ten years of severe epilepsy and that of the postoperative eighteen months or so of convalescence before the patient was permitted to work. The patient's attitude is consistent with the idea that lesions of the frontal lobe affect initiative and planning (Penfield and Evans[9]), but proof of the hypothesis is still difficult.

Thus no defect of social adjustment or of intellectual capacity in K. M. is clearly shown. How is one to interpret the glaring differences between his case and the cases reported by other authors, in which social defects were so obvious? The reader may feel, perhaps, that the psychologic search for defects in K. M. was not competent or not thorough. Must he not have the symptoms found in other patients? But K. M. was able to join the army and remain unnoticed until he had a fit, whereas the patients reported on by other authors have had to be detained and cared for. K. M., therefore, has not the main symptoms presented by other patients. If it is still believed that the examination by laboratory methods was not thorough enough to reveal subtle defects, his grossly superior social adjustment is still to be explained.

Another possible explanation of the differences between K. M.'s case and other cases might be a considerable individual variability in function of the frontal lobe. K. M.'s lack of the expected deterioration could be due to an atypical cerebral organization. This possibility cannot be ruled out; one can only say that the reverse assumption has been made by every student of cerebral function.

However, before one accepts the assumption of such great individual variability, one must examine a third possibility. This is suggested by the fact that K. M.'s operation was for the removal of a specific area of scarring, not for tumor (as in the cases of Brickner,[6] Nichols and Hunt[7] and Karnosh[10]) or for the removal of areas of atrophy with a possibly indeterminate extent (Mixter, Tillotson and Wies[8]). The removal of K. M.'s scar was so done as to minimize further scar formation or a residue of pathologically changed tissue. The possibility exists, therefore, that K. M.'s case is a rare one, in which the effect of surgical removal of frontal lobe tissue is not obscured by the presence of further lesions. There is, in fact, positive evidence in some of the cases reported by other authors that they were not dealing with uncomplicated surgical lesions. The deterioration they describe may have been due to pathologic complication and not to the surgical lesion at all.

The clinical analysis of cerebral function is not so easy as it has sometimes appeared, and I must now draw attention to its difficulties before returning to the published case reports and their divergent conclusions. Although the following discussion (of anatomic and pathologic data and the difficulties of getting normal control data) is in the main concerned with studies of the frontal lobe, the methodologic difficulties it deals with apply in general to any analysis of the effect of surgical lesions, and not to study of a particular part of the brain.

ANATOMIC AND PATHOLOGIC SOURCES OF ERROR

In operations on the frontal lobe there is frequently a deliberately planned and radical removal of cerebral tissue. At first sight, the result is made to order for the analysis of function of this area. But all is not so simple.

Anatomic Data.—The special value of a surgical lesion of the brain is that it may have

6. Brickner, R. M.: The Intellectual Functions of the Frontal Lobes: A Study Based upon Observation of a Man After Partial Bilateral Frontal Lobectomy, New York, The Macmillan Company, 1936.

7. Nichols, I., and Hunt, J. M.: A Case of Partial Bilateral Frontal Lobectomy: A Psychopathological Study, Am. J. Psychiat. **96**:1063-1083, 1940.

8. Mixter, W. J.; Tillotson, K. J., and Wies, D.: Reports of Partial Frontal Lobectomy and Frontal Lobotomy Performed on Three Patients: One Chronic Epileptic and Two Cases of Chronic Agitated Depression, Psychosom. Med. **3**:26-37, 1941.

9. Penfield, W., and Evans, J.: The Frontal Lobe in Man: A Clinical Study of Maximum Removals, Brain **58**:115-133, 1935.

10. Karnosh, L. J.: The Clinical Aspects of Frontal Lobe Disease, J. Indiana M. A. **28**:568-572, 1935.

definite limits and destroy all tissue within its boundaries while the rest of the brain remains intact. If these conditions do not hold, however, there is no superior scientific value of the surgical lesion over pathologic lesions, and localization of function is no more possible in such a case than in a case of brain tumor in which no operation is done. The confusion of early theories, before brain surgery was common, shows clearly the need of basing localization of function on the results of well defined lesions. One might think that surgical operations would provide many such lesions, but the fact is that cases are rare in which one can either (*a*) say definitely what tissue is removed or (*b*) have any assurance that the surgical lesion alone can be taken into account. Clearly, if symptoms are to be ascribed to the removal of tissue from the frontal pole, one must be sure that the removal constitutes the only lesion. But the good cases for psychologic study do not come to autopsy, and without autopsy one cannot be sure that this is true. In the great majority of cases, in fact, it is quite untrue.

Physiologists and psychologists have long recognized in animal experimentation that the only good source of information about the nature of a cerebral lesion is the histologic study of the brain after necropsy. One must usually get along without necropsy data in the clinical study, but this does not mean that the information is less needed. The neat diagrams, published to show just where a surgical excision occurred in clinical cases, are quite misleading in their appearance of accuracy. It is difficult, sometimes impossible, to identify gyri at operation. When growth of a tumor has distorted the brain, any claim to precise localization is nonsense. Further, there may be destruction at a distance, due to tumor growth and compression of the whole brain; and there may be other pathologic changes which the surgeon can recognize, but cannot remove, if they lie within the specialized motor or speech areas or at the base of the brain. For various reasons, the complications of clinical operations on the brain are much more frequent than are those in animal experiments. Little weight would be given to localization of function established by animal experimentation without necropsy data; how can one give more to a clinical study, in which the data are just as necessary?

Of course, some information about the function of the human brain is better than none. The moral is not to abstain from studying clinical material until the perfect case is found, but to regard fallible data as fallible, to make every effort to get as good cases as possible and to put most weight on the cases in which anatomic data are most complete and trustworthy. One must not lump together all cases in which the frontal lobes have been touched by a surgeon and then treat them as a homogeneous group.

It has been pointed out elsewhere (Hebb [11]) that a negative conclusion—the conclusion that a given function is not dependent on a certain cortical region—can often be made with more security than a positive conclusion, since it is easier to determine that a specific area has been removed without producing mental symptoms than that symptoms accompany destruction in one area only. It is well to keep in mind these two aspects of the localization of function. A given hypothesis can be refuted conclusively but can be established only with great difficulty.

Pathologic Disturbances.—So much for the outright destruction of tissue. I come now to the question of the physiologic changes which occur in an area of incomplete destruction. One reason, no doubt, that accompanying pathologic lesions are usually forgotten in selecting cases for study, and in the interpretation of symptoms, is that they tend often to be small and may seem negligible as compared with a large surgical removal. But this assumption overlooks an important fact. The small and diffuse region of partial necrosis can have a greater effect in the production of symptoms than a larger area of complete destruction and cleancut removal of tissue.

Electrophysiologic studies provide a rationale for this otherwise anomalous state of affairs. It is known that spontaneous rhythmic neural activity is induced or modified by changes in the cell mediums, and therefore by changes in the chemical constitution of the cell itself (Fulton [12]). Deficiency of blood supply in the frontier zone of a scar (Penfield and Humphreys [13]) or in an area of increased pressure due to the presence of a cerebral tumor could, obviously, produce such chemical changes. The chromatolysis in an area of incomplete destruction also implies a chemical change within the cells. This, in turn, means a change in the pattern of cellular action. Such a change might occur in many ways, but there is at least one way which would adversely affect function in the rest of the brain. Electroencephalo-

11. Hebb, D. O.: Human Intelligence After Removal of Cerebral Tissue from the Right Frontal Lobe, J. Gen. Psychol. **25**:257-265, 1941.

12. Fulton, J. F.: The Central Nervous System, in Luck, J. M., and Hall, V. E.: Annual Review of Physiology, Stanford University, Calif., Annual Reviews, Inc., 1940, vol. 2, pp. 243-262.

13. Penfield, W., and Humphreys, S.: Epileptogenic Lesions of the Brain: A Histologic Study, Arch. Neurol. & Psychiat. **43**:240-261 (Feb.) 1940.

graphic studies in general show an inverse relation between integrated mental function and the synchronous action of individual cells (hypersynchrony) which is implied by large potentials (Jasper, Kershman and Elvidge [14]). In an area of injury, the electroencephalogram reveals a pronounced increase of synchronous activity appearing as slow waves or spikes, which must have a tendency to act as pacemaker and increase synchronization in neighboring tissue. The perfect example of this is supplied by Dr. Herbert Jasper,[15] who observed a patient with periods of transient aphasia coinciding with the discharge of large potentials from the speech area: Synchronization of cellular rhythm and apparent hyperactivity obliterated normal function instead of increasing it. If hypersynchrony is indeed the negation of integrated function, the effect of neural processes within an area of injury must at times be deleterious in their relation to processes elsewhere.

This reference to intercellular relations is rationalization rather than an explanation of observed clinical phenomena, for the course of events is in part inferred from these phenomena; but it is worth showing that the deleterious effect of pathologic processes, and an actual improvement of mental level following the extirpation of the tissue concerned, is not out of accord with physiologic theory. It had often been suspected that pathologically affected tissue, as such, could interfere with normal cerebral function; but the idea was not given great weight, apparently because there was no rational basis for it and the evidence was not overly clear. The first convincing evidence came only with cases of clean surgical extirpation from the frontal lobes (Jefferson [16]), evidence which was strengthened by drawing attention to the meaning of the concomitant electrical phenomena (Hebb [17]). The same conclusion was arrived at, apparently independently, by Stookey, Scarff and Teitelbaum.[18]

Finally, conclusive evidence that pathologic changes not productive of pressure on the rest of the brain could nevertheless have a detrimental effect on its activity was provided by 2 cases in which improvement followed bilateral removal of an area of atrophy or of scar tissue (Mixter, Tillotson and Wies [8]; Hebb and Penfield [1]) from the frontal lobe. In these 2 cases the patients had epilepsy; but the argument of Jefferson [16] and of Stookey, Scarff and Teitelbaum [18] shows that the same principle may apply in cases of brain tumor.

The importance of the careful removal of pathologic tissue and the necessity of avoiding postoperative scar formation have been stressed by Penfield.[19] His argument, based primarily on neuropathologic data, is strongly supported by the excellent psychologic and behavioral status of patients following operation in which the degree of further scar formation is minimized. In appraising the effect of pathologic destruction as a complication of surgical operation, therefore, one must take account of the physiologic disturbance in cells whose function has been disordered, as well as of the total loss of cells. The pathologic lesion may be small or diffuse, but its size or concentration is not a safe guide to its importance in producing symptoms. It seems, then, that evidence concerning the suitability of a case for the study of localization of function must include electroencephalographic data. The electroencephalographic evidence is as necessary as are anatomic data in the interpretation of symptoms. It is not suggested that the electroencephalogram is infallible; but it is the only index of the physiologic status of cerebral tissue in the living patient, and as such it becomes of the first importance.

It is particularly important in cases of tumor to have good pneumoencephalographic and electroencephalographic data. After removal of a tumor there are often indications of widespread atrophy. The interpretation of such evidence is sometimes disputed, and signs of atrophy may be misleading. Nevertheless there seems to be no doubt that the growth of a large tumor is frequently accompanied by pathologic changes in the rest of the brain. The most likely factor is pressure, but what the cause may be is not important for the present discussion. Also, it may be doubtful whether pressure atrophy necessarily produces psychologic symptoms; but when symptoms are present, the presence of atrophy cannot be disregarded. When a large tumor has been removed, therefore, one must be cautious in at-

14. Jasper, H. H.; Kershman, J., and Elvidge, A.: Electroencephalographic Studies of Injury to the Head, Arch. Neurol. & Psychiat. **44**:328-350 (Aug.) 1940.

15. Personal communication to the author. Dr. Jasper points out that hypersynchrony per se is not necessarily what prevents normal function, since the refractory states of the tissue must also be taken into account. What is important for the present discussion is the empiric fact that integrated function vanishes as synchronous activity increases.

16. Jefferson, G.: Removal of Right or Left Frontal Lobes in Man, Brit. M. J. **2**:199-206, 1937.

17. Hebb, D. O.: Intelligence in Man After Large Removals of Cerebral Tissue: Report of Four Left Frontal Lobe Cases, J. Gen. Psychol. **21**:73-87, 1939.

18. Stookey, B.; Scarff, J., and Teitelbaum, M.: Frontal Lobectomy in the Treatment of Brain Tumors, Ann. Surg. **113**:161-169, 1941.

19. Penfield, W.: Epilepsy and Surgical Therapy, Arch. Neurol. & Psychiat. **36**:449-484 (Sept.) 1936.

tributing psychologic symptoms to the surgical excision alone (Dandy [20]).

Anatomic and Pathologic Conclusions.—From all these considerations, several conclusions may be drawn concerning the case material that is suitable for the localization of function.

1. Cases of injury to the brain—atrophic, neoplastic or traumatic—for which operation is not performed cannot be used, with possible rare exceptions. Neither the minimal nor the maximal extent of outright destruction can be determined, nor can the probable effect of physiologic dysfunction be evaluated.

2. Cases in which intracranial tumor has been removed are rarely satisfactory. In some instances it may be possible to determine the minimal extent of surgical destruction; if so, negative conclusions may be justified. Positive conclusions can be established only if the maximal possible destruction is known and is limited to a specific area and if physiologic dysfunction is ruled out. These conditions are practically never met in operations on large tumors.

3. In practice, surgical procedures are always more or less complicated by pathologic changes in the part of the brain that remains after operation, and one has no way at present of knowing the effect of such changes in the individual case. Of two cases in which identical surgical removals have been made, but with pathologic complications of varying effects, the one in which the fewer symptoms occur is the one which most clearly shows the effect of the surgical removal alone. Consequently, this principle may be stated: The case in which the fewest symptoms follow a known surgical removal is likely to be the one in which the truest picture of the effect, or lack of effect, of the removal is given, and for the localization of function the most weight must always be given to such a case.

MISUSE OR LACK OF NORMAL CONTROL DATA

If some of the statements about anatomic data seem obvious, just as obvious are certain facts about normal control data, which nevertheless need to be emphasized again. One cannot use school children as normal control subjects for adults, or college students for the middle-aged, or academic and clerical workers for farm populations. Yet when normal control subjects are used at all, it is frequently in just such a way.

It is not generally appreciated that an adequate normal control group is extremely hard to obtain in clinical studies of adults. Intelligence test norms are data from a normal control group and may be used as such as long as the clinical subject comes from the same population. Unfortunately, the test data are usually obtained from school children and are not applicable to adults. To some workers, apparently, this appears to be a trivial point—legitimate, but unimportant. On the contrary, a review of the published cases indicates that failure to find adequate normal controls has repeatedly led to serious error.

An intelligence test which has been standardized with adult subjects is the Wechsler-Bellevue scale.[21] At first glance, this test seems to supply the normal control data that are needed for analysis of adult clinical performance. But there are still difficulties, such as the low reliability of the subtests of the scale, which makes it practically useless for a small group of subjects, and the limited range of material which the test provides. Another difficulty is less obvious, but greater. Wechsler has provided no information whatever about the original selection of subjects. Nearly 2,000 subjects were tested in the first place; and the choice of records from this pool, to determine test norms, was a model of the sampling process. But any one who has tried to obtain the consent of subjects chosen at random from the general population, even when they are out of work and are to be paid for being tested, knows how difficult it is to avoid a high percentage of refusals. In some circumstances refusals can result in a marked bias. The utmost care, diplomacy and patience must be continually exercised with adult subjects to obtain their original consent and to have them complete the testing process. It is not at all clear how the extremely large number of cases in Wechsler's original pool could have been obtained without the danger of bias running through the whole group. If there is a bias, multiplication of cases will not offset it in the least, and nothing in Wechsler's later procedure would eliminate it. It is known that the range of ability within any one occupational group is great, and stratification by occupation would not eliminate a selection that might have affected every stratum in the same way. Before the test norms can be used as normal control data, more information is necessary about the original selection of subjects and the way in which so many adults, supposedly chosen at random, were induced to cooperate in the study.

As to the use of child norms with adults, an illustration will show how real the dangers are.

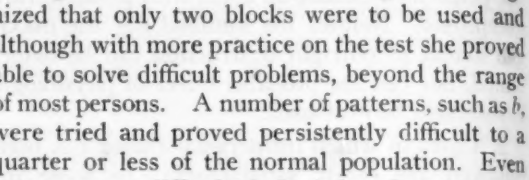
20. Dandy, W. E.: Physiologic Studies Following Extirpation of the Right Cerebral Hemisphere in Man, Bull. Johns Hopkins Hosp. **53**:31-51, 1933.

21. Wechsler, D.: The Measurement of Adult Intelligence, Baltimore, Williams & Wilkins Company, 1939.

Nichols and Hunt [7] report a "marked deficit" as demonstrated by the Knox cube test in a 45 year old man, whose score was no better than the average 7 or 8 year old child's. For a former college student with a good record and a present Otis intelligence quotient of 120, this sounds indeed like a low score. But it happens that Weisenburg and McBride [22] have provided norms obtained with adults. The patient's score is not below the adult range, but near the lower quartile; and since the discrepancy between the data for adults and those obtained with school children suggests a pronounced loss of the ability with age, the patient's score may be relatively still higher when his age is taken into account. Another instance: Brickner [23] refers to his adult patient, who had a Stanford-Binet mental age of 12 years and 9 months, as making the score of a child. The Army data of 1917 and the later study by Weisenburg, Roe and McBride [24] show that such an interpretation, which is based on Terman's data obtained from school children, is quite wrong; the mean adult score on the 1916 revision appears to be between 13 and 14 years, and the score for Brickner's patient is lower than the mean by less than one-half the standard deviation (Weisenburg, Roe and McBride,[24] pages 9 and 59).

The failure to obtain normal control data of any kind, as in Goldstein's work, or the dependence on age norms for school children seems often to be based on the silent assumption that one knows how the "normal" adult will deal with the test problem or that a given test is so simple that any normal adult would succeed with it. No assumption could be more dangerous. One's ideas of the average intelligence are colored by one's occupation, cultural background and familiarity with the abstract and academic.

The divergence between what might be expected and what actually is done by normal persons can best be illustrated by data obtained from a test which has not been published. The test material consisted of shapes cut out of cardboard and five identical wooden triangles with which the cardboard patterns were to be reproduced, two or more being used for each pattern. In the figure, several of the test patterns and some of the solutions are represented. The significant fact is that no pattern could be devised which was so easy that all patients in the public wards of a general hospital would succeed with it in one minute, even though other tests showed that one was not dealing with a population of mentally deficient persons. Some of the failures were almost incredible. An extremely intelligent technician, who was a college graduate and a biochemist, was unable to reproduce pattern *a* in the figure in two minutes, although she recognized that only two blocks were to be used and although with more practice on the test she proved able to solve difficult problems, beyond the range of most persons. A number of patterns, such as *b*, were tried and proved persistently difficult to a quarter or less of the normal population. Even pattern *c* was difficult; in both *b* and *c* many subjects apparently could not keep the orientation of the two blocks distinct. Although they knew that the task was to reproduce the pattern exactly, they would make pattern *d*, perhaps, for pattern *c*, or even pattern *f* for pattern *e*. Such persons often could not see just where the trouble was when they were told that the solution was not satisfactory. Finally, such solutions as making pattern *h* for pattern *g* were observed not once but a number of times; the subject would finish the arrangement of blocks and, incredibly, ask whether it was right.



Test problems and representative failures made by normal subjects. Diagrams *a*, *b*, *c*, *e* and *g* represent patterns cut out of cardboard and placed before the subject, who was to reproduce the pattern with wooden blocks in one minute. Broken lines inserted in diagrams *a*, *b* and *g* show how the blocks were placed in a correct solution, but these lines were not given in the test patterns. The subject was given five identical wooden triangles (with 30, 60 and 90 degree angles) and was told to use as many as he needed to make an exact copy of the cardboard pattern. The hatched diagrams represent solutions of a kind made by a fifth or more of the normal population: *d* is an attempted copy of pattern *c*; *f*, a copy of pattern *e*, and *h*, a poor attempt to copy pattern *g*.

These are of course extreme examples, but they illustrate a kind of ineptitude in solving abstract problems that is to be observed in less degree with a number of tests and among persons who have no defect of economic and social adjustment and whose Binet score may be within normal limits. If the described behavior were an

22. Weisenburg, T., and McBride, K. E.: Aphasia: A Clinical and Psychological Study, New York, Commonwealth Fund, 1935.

23. Brickner, R. M.: An Interpretation of Frontal Lobe Function Based upon the Study of a Case of Partial Bilateral Frontal Lobectomy, Research Nerv. & Ment. Dis., Proc. **13**:259-351, 1934.

24. Weisenburg, T.; Roe, A., and McBride, K. E.: Adult Intelligence: A Psychological Study of Test Performances, New York, Commonwealth Fund, 1936.

isolated instance, it could be dismissed; but it was observed repeatedly with this test. No one, I think, will find it credible; and this means that if one found such behavior in a case of cerebral damage, and had no test data from unsophisticated adults, one would be bound to conclude that the behavior was determined by the presence of the lesion. There is an obvious similarity of the test to some of Goldstein's (Bolles and Goldstein [25]), for which no normal control data are provided.

In subsequent work, with the object of getting improved test instruments for the unsophisticated adult, I have tested approximately 300 patients in the public wards. Instead of composite tests, separately standardized ones were used, some of which were especially designed to avoid literary and academic sophistication. If by "intelligent" one means making an average score in a number of intelligence tests, then it may be said that an intelligent person with no suspicion of cerebral injury or disease may do very badly, or may give apparently very stupid answers, in a single kind of test or on individual test items. Such test material tends to be eliminated in the standard composite tests by the ordinary routine of item selection, but in special tests which have not been standardized there is a real danger of assuming that a variation from the norm which is frequently obtained for the normal population can be due only to the effects of cerebral injury. It need hardly be added that such variability is less likely to appear in an academic population and that neither school children nor college students make an adequate control group for older subjects or for persons not engaged in clerical work.

The work of Weisenburg and McBride [22] and of Weisenburg, Roe and McBride [24] with normal subjects seems strangely unheeded. For any one who is proposing to set up a test battery for clinical analysis of cerebral function, these authors have provided the groundwork of normal control data. Dr. Morton and I have also attempted to supplement their test battery (Hebb,[26] Hebb and Morton [27]) and to give a greater variety of tests in which roughly satisfactory adult norms are provided.

25. Bolles, M., and Goldstein, K.: A Study of the Impairment of "Abstract Behavior" in Schizophrenic Patients, Psychiatric Quart. **12**:42-65, 1938.

26. Hebb, D. O.: Verbal Test Material Independent of Special Vocabulary Difficulty, J. Educ. Psychol. **33**: 691-696, 1942; Footnote 26.

27. Hebb, D. O., and Morton, N. W.: The McGill Adult Comprehension Examination: "Verbal Situation" and "Picture Anomaly" Series, J. Educ. Psychol. **34**: 16-25, 1943.

REVIEW OF CASE REPORTS

UNILATERAL "LOBECTOMY"

There are thus two hurdles for investigators who would attempt to show that defects result from simple loss of frontal lobe tissue. One is to determine the size and locus of the surgical lesion and to verify the absence of significant pathologic changes which complicate the picture. The second is to obtain normal control data. Criticism on both scores is relevant to much published work. In the following review, published reports of removal of the frontal lobe are evaluated with respect to the adequacy of such anatomic and behavioral controls.

Negative Conclusions.—The difficulty with anatomic and pathologic controls is in general less for the investigator who attempts to show that a given defect does not follow frontal lobectomy. It has already been pointed out that the minimal extent of a lesion is usually easier to determine than the possible maximal extent. The anatomic data of Jefferson [16] and Lidz,[28] who concluded that no defects follow unilateral lobectomy, might be suspect, however, for in removal of a tumor the destruction of normal tissue may seem to go farther back than it actually does. However, the reverse is true of atrophy and scar formation, and the results reported by Hebb [29] in 5 cases of removal of scars confirm the conclusions of Jefferson and Lidz.

None of these studies, including my own, utilized good normal control data but depended either on high postoperative scores or on comparisons of preoperative and postoperative scores in concluding that loss of frontal association areas has no detectable effect on test scores. Emphasis here is on the word "detectable"; a better conclusion would be that no defect has been demonstrated. For comparison of preoperative and postoperative scores is not valid except to show that a surgical removal from the frontal lobe leaves intelligence as high as, or higher than, that with a pathologic lesion. Obviously a high preoperative score might have been still higher if the cerebral tumor or scar had not occurred in the first place. From these papers, and from that of Stookey, Scarff and Teitelbaum,[18] several conclusions are justified: (1) A high level of functioning is possible after unilateral frontal lobectomy; (2) no clinically evident defects need follow, and (3)

28. Lidz, T.: A Study of the Effect of Right Frontal Lobectomy on Intelligence and Temperament, J. Neurol. & Psychiat. **2**:211-222, 1939.

29. Footnotes 11 and 17.

tests fail to demonstrate any loss of intellectual ability after the unilateral surgical removal of frontal lobe tissue when pathologic complications are minimized.

Attempts at Localization (Positive Conclusions).—Of the various attempts to show that surgical lesions of the frontal association areas produce definable defects, Rylander's [30] study is unique in actually using a carefully chosen normal control group. As a result, it provides important and extremely interesting psychologic information concerning the sequelae of removal of tumors of the frontal lobe. His study would have been beyond criticism if he had concluded only that the defects, some of them so slight as to be demonstrable only by group comparisons and not in the individual patient, were those that characterize the postoperative course after removal of tumor. It is an undoubted fact that the removal of a large tumor is likely to leave the patient with more or less pronounced mental changes, and Rylander's excellent method adds definite information about their nature. But he went further and reached the conclusion that the defects which he described were due to the surgical excision of frontal lobe tissue. No such conclusion is justified. As has already been seen, the removal of a tumor may not leave the rest of the brain in a normal condition. Further, in his 32 cases Rylander included 1 case in which the anterior cerebral artery was believed to have been clamped at operation, cases in which a tumor could not be completely removed and cases in which the tumor was of a type which could be expected to recur. Here, the described mental and moral defects may be due to the surgical removal, to the added pathologic destruction or to both; but they cannot be put down simply to the uncomplicated loss of frontal lobe tissue.

In another study on a large group, Halstead [31] encountered this difficulty, as well as the problem of getting normal control subjects. Halstead's data present no evidence that his cases were any more suitable than are most cases of tumor for the localization of frontal lobe function; the inclusion of cases of incomplete removal of tumor, of glioblastoma (a rapidly recurrent type of neoplasm) and of hemiparesis or aphasia not accounted for by the extent of the surgical lesion means that the patients had serious pathologic as well as surgical lesions; and defects cannot be unambiguously ascribed to the surgical removals. The inclusion of cases of aphasia with the cases of lesions of the frontal pole further complicates interpretation of the group scores.

As to the control group, Halstead gave no data except to state that the ages of his 11 normal subjects ranged from 12 to 56 years. The patients with lesions of the frontal lobe, on the other hand, were all adults, from 31 to 63 years of age. The actual distribution of ages of the normal subjects is not known, and any information about their occupations and degree of education is lacking. Since the clinical subjects included an unskilled laborer, a farmer and a truck driver, one cannot be sure that the comparison of normal subjects and patients with lesions of the frontal lobe is valid with respect either to age or to sophistication.[32] More data are necessary before one can be sure that the quantitative defects are characteristic even for patients with removal of the frontal lobe with pathologic complications.

Other reported cases need not be examined in so much detail. German and Fox,[33] Penfield and Evans [9] and Ackerly [34] described defects clinically evaluated and did not depend for their positive conclusions on test methods. In no case is there reason to be sure that the pathologic conditions were suitable for the localization of function, although, as in Rylander's monograph, data of considerable psychologic significance are given.

BILATERAL "LOBECTOMY"

There have been a number of cases of bilateral removal of the frontal association areas. From this number can be excluded such cases as Ackerly's, in which the surgical destruction was unilateral and the second lobe was pathologically

30. Rylander, G.: Personality Changes After Operations on the Frontal Lobes: A Clinical Study of Thirty-Two Cases, London, Humphrey Milford, 1939.

31. Halstead, W. C.: Preliminary Analysis of Grouping Behavior in Patients with Cerebral Injury by the Method of Equivalent and Non-Equivalent Stimuli, Am. J. Psychiat. **96**:1263-1291, 1940.

32. Age differences also invalidate the comparison of patients with lesions of the frontal lobe and other patients. The average age of the group with lesions of the frontal lobe was 44.2 years (range, 31 to 63 years); the average age for the other patients, 27.7 years (range 15 to 35 years, with 1 patient 51 years of age). The difficulty is even greater with the data of Halstead and Settlage (*Arch. Neurol. & Psychiat.* **49**:489-506 [April] 1943), in which 3 patients aged 31 to 51 years with lesions of the frontal lobe are compared with 3 patients 19 to 25 years old with lesions of other parts of the brain. The type of behavior studied is affected by age; we do not know, therefore, whether the lower scores for patients with lesions of the frontal lobe are due to the locus of the lesion or to age.

33. German, W. J., and Fox, J. C.: Observations Following Unilateral Lobectomies, Research Nerv. & Ment. Dis., Proc. **13**:378-434, 1934.

34. Ackerly, S.: Instinctive, Emotional and Mental Changes Following Prefrontal Lobe Extirpation, Am. J. Psychiat. **92**:717-728, 1935.

involved, with no surgical attempt to remove an area of possible dysfunction. As has been seen, in such cases positive localization of function is no more possible than if there had been no surgical intervention at all.

The first case of bilateral surgical removal described is that of Brickner,[35] who arrived at the conclusion that his patient had "a single, basic intellectual deficit," which he called a loss of synthesis. There are theoretic difficulties about this concept which will be discussed in a later section. Clinically, there were serious social abnormalities in this case, and Brickner and many subsequent writers have attributed these defects to a simple loss of tissue. There is no sufficient basis for the conclusion. First is the known fact, already stressed, that large tumors tend to be accompanied by pathologic changes in the rest of the brain. The surgeon's report at operation confirms the probability of widespread damage and makes it clear that little was known of the status of the remaining brain tissue after operation. Veins were observed to be thrombosed before the operation began, and it is not stated that the preoperative thrombosis was only in the tissue removed. Much of the field of operation could not be seen by the surgeon at all. Although the line of section was far back, one anterior cerebral artery was not seen, nor apparently the other; so either artery may have been thrombosed or shut off at operation. The deeper parts of the tumor were dissected out with a finger, without visual guidance. Necrotic tissue could hardly have been cleaned up, so that scar formation may have resulted; and the postoperative course of repeated epileptic fits is confirmatory. Further, the patient's postoperative deterioration appears to have fluctuated rather greatly. If so, the cause could not have been a static loss of tissue but is likely to have been related to the epilepsy. Electroencephalographic studies show clearly that epileptoid dysfunction can occur distinct from actual convulsions. Mental slowing without any obvious objective sign of an attack has also been described (Hunt, Wittson and Harris[36]; Hebb and Penfield,[1] page 431). In his latest report on the case of bilateral "lobectomy," Brickner[35a] has described increased irritability for a full day preceding an epileptic attack, a symptom which suggests strongly that it, and other fluctuations of social adaptation, arose from epileptoid states, even when an actual convulsion did not follow. The case is that of a deteriorated epileptic patient with a large removal of the frontal lobes but, also, with an unknown degree of pathologic destruction in the rest of the brain. In such a case there is no evidence whatever as to the effect of a similar removal of frontal lobe tissue without pathologic complications.

Another extensive study of a case of bilateral removal of a tumor was reported by Nichols and Hunt.[7] Like Brickner's, their patient was undoubtedly deteriorated. However, their attempt to define the nature of the loss more exactly by the use of tests cannot be considered successful, for their patient was 45 years old and they drew their control data from college students and from children's mental age norms. Their interpretation of results with the Knox cube test has already been referred to. A mental age score of 7 years sounds like a definite loss for a formerly intelligent adult, but it is actually well within the range of adult scores (Weisenburg and McBride[22]) and cannot be evaluated at all before one has norms not merely for adults but for adults in the later decades of life.

In this case, too, there are grave difficulties concerned with the pathologic data. Tumor tissue was left in the middle fossa, and in the report no consideration is given to the lasting effects of pressure before operation. Freeman and Watts[2] (page 68) have quoted Nichols as saying that the presence of air in the region of the chiasm, in a postoperative pneumoencephalogram, showed that no pressure from the tumor remained in this region. What this report neglects is the effect of earlier pressure in the supraoptic or the hypothalamic region, in which atrophy might have occurred. In the encephalogram published by Nichols and Hunt there was evidence of pronounced atrophy and regrowth of tumor tissue.[37] Social and intellectual defects can as well be related to these pathologic conditions as to the surgical excision. Like Brickner's case, the case of Nichols and Hunt shows clearly that lasting deterioration may follow the removal of a large and compressing tumor from the frontal region; it gives no good evidence as to the effect of extirpating frontal association areas in more favorable circumstances.

In the case described by Mixter, Tillotson and Wies,[8] an apparently conservative extirpation of atrophied tissue from both frontal lobes was followed by notable improvement and later relapse. The conclusions drawn by the authors were negative; that is, they did not ascribe symp-

35. Brickner, R. M.: (*a*) Bilateral Frontal Lobectomy: Follow-Up Report of a Case, Arch. Neurol. & Psychiat. **41**:580-585 (March) 1939; (*b*) Footnote 23; (*c*) Footnote 6.

36. Hunt, W. A.; Wittson, C. L., and Harris, H. I.: Temporary Mental Impairment Following a Petit Mal Attack, J. Abnorm. & Social Psychol. **37**:566, 1942.

37. In a personal communication, Dr. Nichols reports pronounced electrical abnormalities recorded from the residual tissue of both frontal lobes.

toms to the surgical removal. The fluctuation of symptoms, with recovery first and then relapse, shows at least that the defects which disappeared temporarily are to be ascribed to a variable physiologic condition and not to the permanent surgical removal. Gibbs, Gibbs and Lennox [38] reported improvement in the electrical record after operation in this case, and it seems quite possible that, as Freeman and Watts have suggested, a more radical removal might have had better results, particularly if it had been possible to keep postoperative scarring to a minimum.

Other cases may be referred to briefly. Karnosh [10] described a case in which operation was performed for tumor of a type which tended to recur, and Gantt [39] reported 2 cases, in 1 of which, however, there was atrophy or congenital absence of one frontal lobe instead of surgical removal. Both reports described serious deterioration, but there is no reason to believe that the pathologic situation was suitable for interpretation of the normal function of the frontal lobe.

With the exception of the cases reported by Hebb and Penfield and by Mixter, Tillotson and Wies, in both of which improvement is reported to have followed operation, all bilateral operations on the frontal lobe have been done for brain tumor, and in such cases the odds are strongly against the clearcut removal that is needed for the analysis of function. In the cases of tumor in which adequate data are provided there are positive indications of serious pathologic involvement. Even in the case reported by Mixter, Tillotson and Wies it must have been difficult to know how far posteriorly the region of atrophy extended, and the postoperative course indicates strongly that the remaining brain tissue was pathologically involved.

In contrast to these pathologic conditions is the clearcut line of section shown by postoperative pneumoencephalograms in Hebb and Penfield's case and the absence of any great amount of atrophy. There were still occasional abnormalities in the electroencephalogram, but in general the part of the brain which remained after operation was as undamaged as one could hope for in a clinical case. An exceptional lack of psychologic abnormality accompanied this exceptional absence of pathologic change. It is unlikely that the two facts are not related.

38. Gibbs, F. A.; Gibbs, E. L., and Lennox, W. G.: Cerebral Dysrhythmias of Epilepsy: Measures for Their Control, Arch. Neurol. & Psychiat. **39**:298-314 (Feb.) 1938.

39. Gantt, W. H.: Impairment of the Function of Adaptability as Measured by a Simple Conditioned Reflex Test in Certain Psychogenic Contrasted with Organic Diseases, South. M. J. **31**:1219-1224, 1938.

FREEMAN AND WATTS'S INTERPRETATION BASED ON FRONTAL LOBOTOMY

Freeman and Watts [2] have based an elaborate psychologic interpretation of function of the frontal lobe on the study of a series of 80 cases of "lobotomy," an operation in which most of the fibers connecting the frontal association areas with the rest of the brain are cut. Their theory of loss of foresight resulting from injury to the frontal lobe will be discussed in a later section. More important for the present is the authors' initial assumption that the temperamental changes in their patients are deficit phenomena.

Now the evident fact is that the operation they describe must produce fairly extensive pathologic changes. Once again one is dealing with a purely surgical procedure complicated by pathologic changes, without anything which permits one to eliminate the latter as a source of symptoms. Most significant, in this respect, are the instances of recovery with later relapse following the same form of operation which produced a number of lasting recoveries (Freeman and Watts,[2] page 81).

The question here is: What produced a transient recovery and yet permitted relapse? The cut fibers in the frontal lobes do not regenerate. Some recoveries must have been due to a reversible process, and therefore others may also. As in the similar course which is seen more often with shock therapy, there is suggested a correlation between recovery and a sometimes transient, but with lobotomy more often a chronic, physiologic disturbance. Electrical evidence and the clinical course after the excision of small areas near a sensory or motor region show clearly that surgical procedures are followed by a local cerebral disturbance which may have effects at some distance and which usually disappears slowly during a period of weeks or months. Freeman and Watts' observation (pages 206 to 207) that a characteristic frontal lobe syndrome appears after operation and then slowly disappears, leaving less exaggerated chronic symptoms, is further evidence that some symptoms referable to the frontal lobe are a product of physiologic disturbance. If lobotomy tends to leave extensive scar formation and vascular damage, the physiologic disturbance could become chronic, although diminished presumably from its higher level immediately after operation.

Intrinsically, this may be a less likely explanation of personality changes than that an essential tract is interrupted by lobotomy. Yet it is to be remembered that the abnormalities of personal adjustment in the cases reported by Freeman and Watts were highly variable and that, as will be

seen later, their attempt to reduce the disturbance to a single defect (of foresight with respect to the self) is neither psychologically acceptable nor in agreement with a number of their case histories. The variation from one case to another suggests, at least, a complication of the surgical incisions by various pathologic lesions. Further, the tactlessness and release of malice which the authors describe did not occur during the period of improvement in Hebb and Penfield's patient, or apparently either in the patient whose case is reported by Nichols and Hunt or in the one described by Mixter. Tillotson and Wies. If the defects described by Freeman and Watts are deficit phenomena, and are not due to cerebral dysfunction, they should occur with lobectomy as well as with lobotomy.

There have been a good many other references in the literature to lobotomy, a discussion of which is not within the scope of this paper. The criticisms that apply to the attempt by Freeman and Watts to analyze normal functions of the frontal lobe on the basis of the clinical phenomena of lobotomy apply also to similar attempts by other authors. Prefrontal lobotomy is a landmark in psychiatric therapy but has yet to provide any interpretable evidence concerning what goes on in the normal frontal lobes.

THEORETIC INTERPRETATIONS OF FUNCTION OF THE FRONTAL LOBES

In a number of instances authors have tried by a single concept to explain the defects observed in cases of operation on the frontal lobes, and thus to achieve a theoretic statement of the functions of the frontal association areas. In discussing three of the most important formulations one may show at least the difficulties to be encountered in such an attempt.

Brickner [23] has tried to show that his patient with the bilateral operation on the frontal lobes had "a single, basic intellectual deficit," referred to as a loss of the power synthesis of "simpler thought processes" into "more complex structures." Freeman and Watts have devised a somewhat more elaborate theory, to the effect that the frontal lobes are concerned with foresight while the rest of the brain mediates intelligence and memory of the past. The foresight associated with the frontal lobes is particularly with respect to personal acts and "the relation of the self to the self" (Freeman and Watts,[2] page 298). Goldstein and Katz [3] ascribed all defects referable to the frontal lobe to a "loss of abstract behavior." Differing as these three concepts do, they have one thing in common when they are applied to the explanation of the clinical phenomena. They explain at once too much and too little. They are too broad and ill defined to be meaningful, and they are too likely to lead to an *ad hoc* interpretation of symptoms. The attractiveness or plausibility of such formulations is part of their danger; it is too easy to think of all the facts they account for and not to ask whether there are others which they do not explain or whether symptoms are absent which they require.

In Brickner's case there were certainly defects of learning and memory, or of association, and a good argument is made for regarding other things, too, as a loss of "synthesis." Yet there are many defects which the patient did not have and which might have been expected to be apparent psychologically from the same loss. The concept will not advance scientific knowledge until it is made less inclusive and its implications more specific, so that it can be tested empirically.

Freeman and Watts' theory of foresight with respect to the self seems actually not to arise from a satisfactory generalization of their data but to be based on the remark of 1 patient (Freeman and Watts,[2] page 120). The lack of foresight after lobotomy is supposed to be seen in tactless remarks and inappropriate acts; but apparently many of their patients had no regrets about such things after they were done, though regret would be implied if the tactlessness occurs only because the effect of a remark is not foreseen in advance. The authors' stress on the freedom from self consciousness that follows lobotomy suggests that many patients were no more concerned about inappropriate acts in the past than in the future. Finally, the frequent freedom from remorse and feelings of guilt after lobotomy seems to have no relation at all to the postulated functions of the frontal lobe, and in general one can say that the variety of postoperative changes described is greater than one would be led to expect from a lack of "foresight with respect to the self."

Goldstein's concept of "loss of the abstract attitude," or of "abstract behavior," is also open to the objection that it includes too much and too little. Behavior that seems to involve abstraction is called concrete and vice versa. Take as an example the copying of a V made with small wooden sticks. The patient makes instead an inverted V, which he says represents the eaves of a house. This is called concrete behavior. But to see an inverted V as a housetop involves abstraction, and it would surely be more concrete to respond to the configuration of the actual objects in front of the patient. What is really described seems to be a shift from one kind of abstraction to another. The fact that not only

signs of damage to the frontal lobe (Goldstein [40]) but amnesic aphasia (Goldstein [41]) and schizophrenia (Bolles and Goldstein [25]) can be reduced to a "loss of the abstract attitude" illustrates well the vagueness and inclusiveness of the term, which can have no value until one knows more precisely what defects are not included. One cannot very well treat three quite different deteriorations as due to a single basic deficiency without accounting for differences, as well as similarities.

In defending his theoretic conceptions, Goldstein [40] thoroughly confused the issues with which the present paper deals. For clarity, his criticism, particularly of Hebb and Penfield,[1] must be considered in detail.

To begin with, his discussion contains errors of fact. 1. He [40] (page 201) assumed that there were no preoperative defects in K. M., the patient who lacked both frontal poles, and stated that his theory would have to be reconsidered if there had been characteristic defects. Dr. Penfield and I thought we had stressed the preoperative defects: Certainly the patient lacked initiative, foresight and ability to handle new tasks, which Goldstein has listed as characteristic clinical signs of destruction in the frontal lobes. 2. Goldstein [40] has stated (page 192) that my failure to find psychologic shortcomings after unilateral operation on the frontal lobe (Hebb [17]) can be dismissed because I did not use the right tests for finding them. But the Arthur performance scale includes the Kohs block design and feature profile tests, used by Bolles and Goldstein [25] as a test of the abstract attitude; and the Stanford-Binet diagrams to be copied from memory are not different from Goldstein's except that they are much more difficult. The patients, including K. M., with bilateral damage did well on these tests. Moreover, K. M. was given a sorting test, the importance of which Goldstein has stressed, and spontaneously sorted objects according to (*a*) use, (*b*) size and (*c*) material (metal, paper, wood, glass): a total of three principles of classification, while the average for normal persons is two and three-tenths (Rylander [30]—the only available norm). 3. Goldstein speaks of K. M. as "admittedly not normal." What Dr. Penfield and I admitted was that the most rigorous search had discovered no defects in the patient, though we knew that this did not prove he had none. It is worth noting that Nichols and Hunt, also, using Goldstein's tests, failed to find loss of the abstract attitude in their patient with bilateral damage to the frontal lobes.

One must object on logical grounds to Goldstein's [40] emphasis on cases which support his interpretations and his disregard of those which are opposed (pages 189 to 192) and to his statement that negative findings "cannot ask for great consideration if the characteristic changes have been found in many other cases." The argument must be completely reversed. As I have tried to show in discussing the difficulties of getting satisfactory anatomic and pathologic data, it is the cases with fewest symptoms to which attention must be paid, since they are the ones in which the effect of pathologic complications is likely to be least. The "many other cases" to which Goldstein refers are the very ones which have been shown in this review to involve pathologic as well as surgical lesions, while the negative cases which Goldstein rejects are the ones in which operation was done to remove pathologically affected tissue.

Finally, one may consider Goldstein's interpretations of the improvement in K. M. following extirpation of both frontal poles. Goldstein argues, in brief, that the brain which lacks all the frontal association areas may function at a higher level than a brain in which less of this area is removed. The interpretation has some support in observations on other types of defect. A habitual mode of response may be persisted in as long as it is at all possible, although a new mode of response would be more efficient if a complete loss of the old mechanism forced the new adjustment. A patient may continue to use a crippled organ rather than shift to a previously unused one, and make the shift only when use of the injured organ is precluded. Instances cited by Goldstein [42] include the persistent attempt to use a partly paralyzed right hand in writing although the left would be more effective, and the formation of a pseudofovea in cases of complete hemianopsia but not in cases of hemiamblyopia.

In these instances, however, the substitute functions are recognizably different from the original, either in mode of performance or in end result, whereas in the case of K. M. it is impossible to distinguish his intellectual functioning from that of normal persons. There is no evidence that the loss of frontal lobe tissue affects his behavior in any way. To argue, therefore, that a large bilateral removal leads to a higher level of intellectual performance than a smaller loss of tissue (apart from an explanation based on cellular dysfunction) makes two assumptions for which

40. Goldstein, K.: The Mental Changes Due to Frontal Lobe Damage, J. Psychol. **17**:187-208, 1944.

41. Goldstein, K.: The Problem of the Meaning of Words Based upon Observation of Aphasic Patients, J. Psychol. **2**:301-316, 1936.

42. Goldstein, K.: The Organism, New York, American Book Company, 1939.

factual support is lacking: (1) that the intellectual defect which Goldstein regards as characteristic of injury to the frontal lobe are deficit phenomena and (2) that intellectual performance after cleancut "lobectomy" is qualitatively different from the normal. Also, this interpretation of K. M.'s improvement following operation totally disregards definite physiologic and clinical facts, namely, the change in the electroencephalogram, and the disappearance of frequent epileptoid states. These facts alone adequately account for the improvement.

CONCLUSIONS

This paper stresses the failure to find psychologic defects that can be attributed to clean surgical injury of the frontal lobes. To avoid misunderstanding, let it stand as a first conclusion that operations on the frontal lobe are followed by defects in almost all cases. But a second conclusion must be that in almost all cases there are also pathologic changes, sometimes extensive, to complicate the surgical removal. The question that this paper has raised is whether the behavioral defects following operation are the result of the surgical removal or whether they are due to the presence of pathologic changes in the remaining part of the brain.

The evidence on which intellectual and moral defects have been attributed to the surgical removal of frontal lobe tissue is very poor. It has been obtained from (1) individual cases, in which the complication of the surgical lesion by extensive pathologic processes is at least highly probable, and (2) average scores for a number of cases indiscriminately grouped. The averages are affected by the inclusion of demonstrably unsuitable cases, and there is no reason to think that the defects are characteristic of all cases in the group. In the interpretation of scores, both for individual cases and for groups, there has been a repeated misuse of normal control data. The objection to ascribing psychologic changes to a surgical procedure alone, when there are also pathologic processes present, applies in cases of lobotomy as well as lobectomy; and there is evidence in the postoperative course after lobotomy to substantiate the objection. Finally, as I have tried to show, there is no possibility at all of interpreting normal functions on the basis of pathologic cases in which surgical treatment is not attempted.

Sweeping as the conclusion is, therefore, it can only be said that no one as yet has produced convincing support for any of the varied ascriptions of normal function to the frontal association areas of the human brain. No one has proved that any single form of normal behavior is dependent on this part of the brain or that a clean surgical removal of both frontal poles has any effect on behavior.

These statements may be taken as meaning more than they do and must be qualified on two points. In the first place, I do not disparage the value of a number of careful studies as analyses of dysfunction or abnormal behavior, although these studies may not contribute to the specific question of the localization of function. In the reports of Ackerly, Brickner, Goldstein, Nichols and Hunt and Penfield and Evans, and particularly in the monographs of Freeman and Watts and of Rylander, there are analyses of behavior which no student of abnormal psychology can disregard. These studies are informative, just as the study of psychosis is informative. Furthermore, when enough is known of cerebral functioning to permit a physiologic interpretation, the observations in question will assume even more significance.

To qualify my conclusions further, I must emphasize that I do not mean that the frontal lobes have no intellectual or moral function. It must be assumed that the region has an important role in behavior, and there are many possibilities which cannot be ruled out. Failure to prove that it has certain functions does not show that it has none, and there is not the remotest basis for saying that the frontal lobes have, for example, no intellectual functions (as some authors have done). From the postoperative behavior of K. M., one may say that the frontal poles of the brain are not necessary to a good day by day adjustment in society or to a good performance on intelligence tests; but this is a limited statement, especially since cerebral injuries affect the correlation of intelligence test scores and behavior in other situations (Hebb [43]). It is still possible that long term planning and initiative (Penfield and Evans [9]), creative work and capacity for radical readjustment may be notably impaired by lesions of the frontal lobe.

The determination to find defects in performance of laboratory tests after injury to the frontal lobe and the lack of attention to high scores (which actually are reported by most investigators who have used intelligence tests) misses a most important problem. Why is there so little direct evidence of intellectual defect from cerebral damage in any area other than that of speech? I have tried elsewhere to summarize the evidence concerning the intellectual effects

43. Hebb, D. O.: Intelligence in Man After Large Removals of Cerebral Tissue: Defects Following Right Temporal Lobectomy, J. Gen Psychol. **21**:437-446, 1939.

of damage to the mature brain. The mean reported intelligence quotient following cortical extirpations, for example, is 108, a score much higher than the normal for adults (Hebb[44]). In discussing such facts, an explanation was sought in an apparent difference of effect between early and late injury to the brain. Apparently, injury in infancy has a much greater effect on later test scores than one which occurs at maturity. This suggests that extirpation of frontal lobe tissue in the infant would have a greater effect than it has in the adult, and hence that the frontal lobes may be more important in development than in later life. However, this is not true of the frontal lobes alone but can be applied with equal validity to other parts of the cerebral cortex except the speech areas; so an essential problem remains. Even if the hypothesis concerning the difference in effect between early and late injuries proves to be acceptable, there is still the question of the way in which the nonspeech areas of the cortex cooperate with the speech areas in normal intellectual function, and it is unlikely that the special question of the adult role of the frontal association areas will be solved apart from this more general problem.

Therapy.—For the physician or surgeon the chief interest of this study is in its showing that a large bilateral removal of frontal lobe tissue is not inconsistent with an excellent clinical recovery, and in establishing the probability that signs referable to the frontal lobe and behavioral defects following most operations on this region are due to complicating pathologic events, not to the surgical removal.

It is important to stress, also, that behavioral deterioration appears to be more severe or more frequent after operation for large tumors than after other extirpations. The single case of Rylander's in which there seemed to be no deterioration was one of operation for abscess. In Halstead's series, of 26 cases, the highest and fourth highest scores on the "per cent of objects grouped" were made in the 2 cases in which a scar had been removed. In the various reports of bilateral frontal lobectomy, the 2 patients whose operations were for the removal of scars were the only ones who could be freed from detention (Mixter, Tillotson and Wies,[8] Hebb and Penfield[1]). One of the 2 patients had a relapse, but the removal of scar tissue in his case was conservative. Cases of removal of scar tissue include also the extraordinary record of M. M. (Hebb[17]), with an intelligence quotient higher than 152 after amputation of the left frontal pole.

Consequently, radical treatment of a traumatic condition or scar may leave the patient in better condition than might be expected by the surgeon who is more familiar with the sequelae of operations for tumor. A further suggestion implicit in the evidence is that thorough cleaning up of tissue which is necrotic or not well vascularized is important not only for the avoidance of definitive epilepsy (Penfield[19]) but for the general mental status of the patient.

SUMMARY

A patient with bilateral frontal extirpation was observed to have made a good social and economic adjustment six years after operation.

It is concluded that though this patient may show some defect in planning for the distant future, the defect is not clearly demonstrated or shown to be due to the cerebral destruction. There is no defect of foresight for the immediate future as shown by tactless remarks or inappropriate social behavior.

An analysis of methodologic difficulties in getting adequate anatomic, pathologic and normal control data suggests that these problems have not been sufficiently appreciated and have led to error in the interpretation of symptoms referable to the frontal lobes.

A review of published case reports of removal of the frontal lobe indicates that no one has as yet shown that defects follow a simple loss of tissue from man's frontal lobes; the loss must, presumably, have some effect, but it is hard to demonstrate and its nature is not yet clear.

The implications of the evidence for surgical treatment, particularly of traumatic injury, are that social and intellectual defects need not follow an uncomplicated bilateral excision of tissue from the anterior part of the frontal lobes.

Yerkes Laboratories of Primate Biology, Inc.

44. Hebb, D. O.: The Effect of Early and Late Brain Injury upon Test Scores, and the Nature of Normal Adult Intelligence, Proc. Am. Philos. Soc. **85**:275-292, 1942.

POLYCYTHEMIA AS A NEUROSURGICAL PROBLEM

A REVIEW, WITH REPORTS OF TWO CASES

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That polycythemia should present a problem to the neurosurgeon will seem, to many, a novel idea. However, recognition of the remarkably high incidence of complications of the central nervous system associated with polycythemia will show that the possibilities are not so remote as they at first appear. In the fields of general medicine and surgery, differential diagnoses are many, as related both to similar and to dissimilar processes. In neurosurgery, not only is the field itself relatively narrow, but the actual number of differential problems is fewer. The immediate chief concern in cases of intracranial disease is whether or not the patient has an operable condition. The lesions commonly associated with this aspect of the problem include intracranial neoplasms, hemorrhage, abscess, infections, hypertensive cardiovascular disease, degenerative lesions and diseases of the eye producing papilledema. Less common are such conditions as pseudotumor,[1] renal disease with uremia[2] and blood dyscrasias.[3] Polycythemia is a member of the last group. It is the part played by this condition as a differential and operative problem to which we wish to call attention in the following case reports and discussion.

The extreme frequency of lesions of the central nervous system in cases of polycythemia has long been recognized.[4] Of 62 patients with this condition at the Hospital of the University of Pennsylvania in the last fourteen years, marked changes of this nature, ranging from facial weakness to complete hemiparesis or stupor, have been present in 13. All these patients were admitted to the medical wards and were studied as cases of polycythemia, and in no instance was the neurosurgical service asked to see a patient because a tumor of the brain was suspected. The explanation of this lies in the following statement: " . . . the association of polycythemia rubra vera with intracranial neoplasia is an event of the greatest rarity,"[5] and in the fact that all of these cases were recognized and verified instances of polycythemia.

IS POLYCYTHEMIA RELATED TO LESIONS OF THE CENTRAL NERVOUS SYSTEM?

Attention has been called by many writers[6] to the possible occurrence of polycythemia as the direct result of lesions of the central nervous system. In 1927, the disease was produced

From the Department of Neurosurgery, Hospital of the University of Pennsylvania, and the Harrison Department of Surgical Research, University of Pennsylvania Schools of Medicine.

1. Stough, J. T.: Choking of the Optic Discs in Diseases Other than Tumor of the Brain, Arch. Ophth. **8**:821-830 (Dec.) 1932.

2. Cushing, H., and Bardley, J.: Subtemporal Decompression in a Case of Chronic Nephritis with Uremia, with Especial Consideration of the Neuroretinal Lesion, Am. J. M. Sc. **136**:484-504, 1908.

3. Mills, E. S.: Papilledema in Pernicious Anemia, Canad. M. A. J. **32**:546-548 (May) 1935. Schinck: A Case of Choked Disc with Thrombopenia, Ztschr. f. Augenh. **49**:265-280, 1923. Watkins, C. H.; Wagener, H. P., and Brown, R. W.: Cerebral Symptoms Accompanied by Choked Disc in Types of Blood Dyscrasia, Am. J. Ophth. **24**:1374-1383 (Dec.) 1941.

4. (*a*) Adams, L. J.: Polycythemia Vera with Special Reference to Nervous Manifestations: An Analysis of Nine Cases, Canad. M. A. J. **32**:128-132 (Feb.) 1935. (*b*) Brockbank, T. W.: Neurologic Aspects of Polycythemia Vera, Am. J. M. Sc. **178**:209-215 (Aug.) 1929. (*c*) Christian, H. A.: The Nervous Symptoms of Polycythemia Vera, ibid. **154**:547-554 (Oct.) 1917. (*d*) Fucher, T. B.: The Clinical Aspects of Erythremia, Boston M. & S. J. **191**:304-311 (Aug. 14) 1924. (*e*) Horder, T.: Remarks upon Vaquez' Disease with Special Reference to Complications and with Notes of Seven Cases, St. Barth. Hosp. Rep. **59**:153-167, 1926. (*f*) Lucas, W. S.: Erythremia or Polycythemia with Chronic Cyanosis or Splenomegaly, Arch. Int. Med. **10**:597-667 (Dec.) 1912. (*g*) Sloan, L. H.: Polycythemia Rubra Vera: Neurologic Complications, Arch. Neurol. & Psychiat. **30**:154-165 (July) 1933. (*h*) Tinney, W. S.; Hall, B. E., and Giffin, H. Z.: Central Nervous System Manifestations of Polycythemia Vera, Proc. Staff Meet., Mayo Clin. **18**:300-303 (Aug. 25) 1943. (*i*) Watson, J. H.: Polycythemia Vera (Vaquez's, Osler's Disease): A Description of a New Clinical Entity, with a Note on a Method of Estimating the Viscosity of the Blood, Liverpool Med.-Chir. J. **26**: 33-49, 1906.

5. Carpenter, G.; Schwartz, H., and Walker, A. E.: Neurogenic Polycythemia, Ann. Int. Med. **19**:470-481 (Sept.) 1943.

6. (*a*) Baserga, P.: Polycythemia from a Lesion of the Diencephalic Hypophysis, Policlinico (sez. med.) **41**:17-24 (Jan.) 1934. (*b*) Carpenter, Schwartz and Walker.[5] (*c*) Castex, M. R.: Erythrocytosis and Erythremias: Etiology, Physiology and Pathogenesis,

(*Footnote continued on next page*)

experimentally by Schulhof and Mathies [7] by the injection of siliceous earth into the diencephalic region of rabbits. By far the greater number of lesions observed clinically have been those associated with infections and degenerative lesions, such as encephalitis and Parkinson's disease, or pituitary syndromes of the Cushing type, with a miscellaneous scattering of other lesions. In all the cases reviewed by Carpenter, Schwartz and Walker,[5] with 3 exceptions, the diencephalic region was involved. These authors cited 2 cases of their own in which cerebellar hemangioblastoma was accompanied with polycythemia, which disappeared after operation and removal of the lesion.[7a] Their first patient showed mental confusion and weakness. There was bilateral papilledema of 3 D., and the cerebrospinal fluid pressure was 320 mm. of water. The red blood cell count was as high as 7,130,000; the hemoglobin content was 23 Gm. per hundred cubic centimeters. The lesion was found in the right cerebellar hemisphere. The second patient complained of headache. There was bilateral papilledema (marked); the cerebrospinal fluid pressure was 330 mm. of water. The red blood cell count reached 6,500,000; the hemoglobin measured 20 Gm. per hundred cubic centimeters. The lesion was in the left cerebellar hemisphere. In both cases the polycythemia subsided and had not recurred up to the time of the last follow-up observation—in the first case, thirteen months, and in the second case, eight months, after operation. That polycythemia might be the underlying pathologic condition was seriously considered in both these cases. However, the pronounced papilledema and the increased cerebrospinal fluid pressure seemed out of proportion to what might be expected to occur with polycythemia, and ventriculographic examination was done.

A brief review of the other 3 cases cited by these authors shows that Oppenheimer [8] mentioned a case of polycythemia in which a cerebellar medulloblastoma was found at autopsy—no details are given. Salus's [6g] patient had right-sided convulsions, with loss of consciousness and paresis of the right side. There were some acromegalic changes, as well as polyuria, glycosuria and impotence. The red blood cells numbered 6,900,000. Autopsy revealed a sarcoma of the convexity of the left frontal lobe. The patient whose case was described by Meiner [9] had epileptiform attacks, spastic hemiplegia of the left side and symptoms characteristic of involvement of the right frontal lobe. The heart and liver were enlarged. The cerebrospinal fluid pressure was 250 to 300 mm. of water, and there were prominent choked disks. The red blood cell count was as high as 8,500,000; the hemoglobin concentration was 135 per cent. Operation showed a diffuse glioblastoma multiforme of the right postcentral convolution and of the angular and supramarginal gyri. The patient received postoperative roentgen therapy, which resulted in the reduction of the red blood cell count to 5,500,000 and of the hemoblobin content to 85 per cent. Seven months thereafter the spleen became enlarged, and the patient died three months later with a normal blood picture.

To the 5 cases just reviewed, we wish to add 3 more from the literature and 1 of our own, in which a subdural hematoma, instead of a cerebral tumor, was found.

CASE 1.—E. S., a 63 year old white woman, was referred to the neurosurgical service of the Hospital of the University of Pennsylvania on July 21, 1944, with the chief complaint of numbness of the left side of the body and pain at the base of her skull.

The patient had apparently been fairly well until June 1, 1944, when she had a draining left ear. She gave a vague history of having hit the left frontal region of her head on a cupboard door in February, without loss of consciousness. In April 1944, she began to have dizzy spells, in which the room seemed to revolve around her from right to left. One of the attacks lasted two days. During that time she tended to fall to the right whenever she attempted to walk. She had no visual trouble at that time. She complained of a "hot feeling" in her head. On May 20 she noticed that her left foot felt numb and queer; and on May 23, when getting into the bathtub, she found that she could not tell heat or cold with her left foot. One month later, her left hand became numb. On June 1, she had a "thick sensation" in

Prensa méd. argent. **16**:693-713 (Oct. 30) 1929. (*d*) Da Rin, O., and Costa, D. L.: Influence of the Central Vegetative Nervous System on the Blood Picture, Clin. med. ital. **65**:303-345 (April) 1934. (*e*) Ferraro, A., and Sherwood, W. D.: Polycythemia in the Course of Neuropsychiatric Conditions, Psychiatric Quart. **11**: 19-33 (Jan.) 1937. (*f*) Guillain, G.; Lechelle, P., and Garcin, R.: Polyglobulia, With or Without Erythrosis, in Certain Hypophyseal-Tuberian Syndromes, Ann. de méd. **31**:100-114 (Jan.) 1932. (*g*) Salus, F.: Central Nervous Regulation of the Red Blood Picture, Deutsches Arch. f. klin. Med. **175**:214-220 (May) 1933.

7. Schulhof, K., and Mathies, M. M.: Polyglobulia Induced by Cerebral Lesions, J. A. M. A. **89**:2093-2094 (Dec. 17) 1927.

7a. Walker has since reported a third case of cerebellar hemangioblastoma associated with a polycythemia which disappeared after removal of the neoplasm (Walker, A. E.: Neurogenic Polycythemia: Report of a Case, Arch. Neurol. & Psychiat. **53**:251-253 [March] 1945).

8. Oppenheimer, B. S.: Vascular Occlusion in Polycythemia Vera, Tr. A. Am. Physicians **44**:338-344 1929.

9. Meiner, E.: Brain Tumor Complicated by Polyglobulia, Schweiz. med. Wchnschr. **66**:338-339 (April 4) 1936.

her throat and some difficulty in swallowing. At the same time, her vision began to be blurred, and double vision developed. These changes became progressively worse up to the time of her admission. On admission, she was unable to read a newspaper and said she felt as though she were looking through a tunnel. Every time she attempted to sit up in bed she had a severe stabbing pain in the occipital region. There was no nausea, vomiting or generalized headache. She complained of tiring easily and of becoming dyspneic on long walks. Although her appetite had been good, she had lost about 20 pounds (9.1 Kg.) in the past seven months. She complained of chronic constipation. Her face, she thought, had been slightly redder than normal for the past two years. She had never had convulsions.

Physical examination revealed a slightly undernourished woman. She did not seem acutely ill and was fairly cooperative, but showed a tendency to become mentally confused. Her general coloring was a moderately dusky red. The mucous membrane of the mouth and pharynx was conspicuously injected. The chest was entirely normal. The heart was not grossly enlarged; there were no murmurs. The edge of the liver was palpable 4 fingerbreaths below the costal margin. The spleen was not palpable. There was no clubbing of the fingers or cyanosis of the nail beds. The superficial veins of the extremities were tortuous. The blood pressure was 160 systolic and 95 diastolic when she was in supine position. The Kolmer and Kline reactions of the blood were negative. Urinalysis revealed nothing significant. The hematologic findings before and after her admission to the University Hospital are given in table 1.

TABLE 1.—*Hematologic Findings in Case 1*

Date	Red Cells (Cu. Mm.)	Hemoglobin, %	White Cells (Cu. Mm.)	Hematocrit Reading	Miscellaneous Data and Treatment
6/ 1/44	7,350,000	144	8,200	..	270,000 platelets
6/ 6/44	6,910,000	129	.....	..	500 cc. of blood drawn 6/3 and 6/5
6/ 9/44	5,350,000	108.9	8,800	..	500 cc. of blood drawn 6/7
7/10/44	6,820,000	120	.....	..	
7/22/44	6,900,000	120	9,400	72	Patient admitted to University Hospital; ventriculogram 7/27
8/ 2/44	.....	116	11,500	64	500 cc. of blood drawn 8/2 and 8/3
8/ 5/44	.....	102	14,500	54	500 cc. of blood drawn
8/ 7/44	6,500,000	100	17,800	59	
8/10/44	5,800,000	88	18,800	54	
8/17/44	5,000,000	88	14,900	..	
8/18/44	Right frontotemporal craniotomy				
8/21/44	3,700,000	68	16,400	..	
8/24/44	3,800,000	75	15,000	43	
9/ 9/44	.....	72	11,900	..	Patient discharged 9/12
10/ 7/44	5,600,000	98	.....	..	
12/14/44	6,700,000 (?)	86	.....	..	
1/22/45	8,000,000	102.5	6,050	55	Red cells showed achromia and microcytosis

Lumbar puncture revealed that the fluid was clear and the pressure 350 mm. of water. There were 2,000 red blood cells per cubic millimeter. The protein measured 48 mg. per hundred cubic centimeters. The serologic reactions were negative; the colloidal gold curve was 0000000000. The roentgenogram of the skull was normal. A roentgenogram of the chest showed some enlargement of the right and left sides of the heart, with accentuation of the pulmonary markings.

Neurologic examination showed subjective numbness of the left arm and leg and the left side of the trunk. There was definite euphoria, with a tendency to memory defect and slowing of mental activity. The Romberg sign was positive, with swaying to the right. There was intention tremor in the heel to knee test. The knee and ankle jerks on the left side were greatly impaired. There was bilateral papilledema, with a few retinal hemorrhages. Objective sensory changes were confined

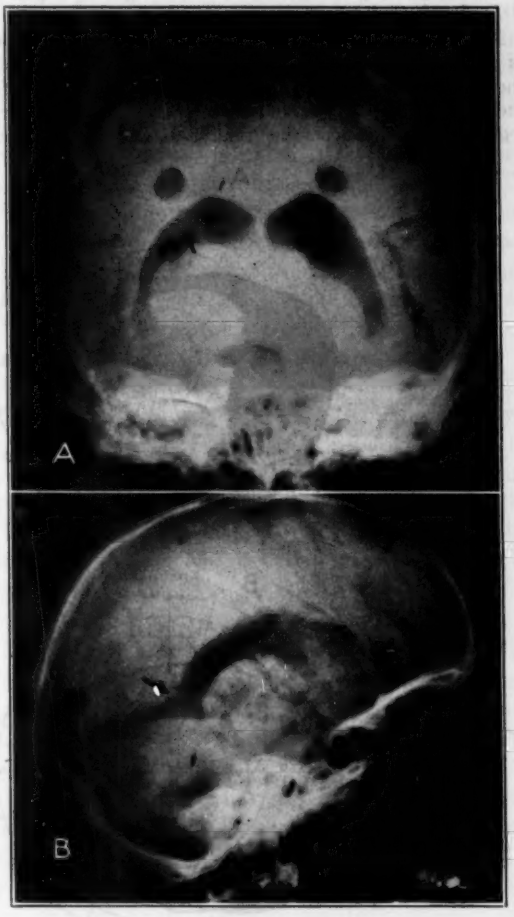

Fig. 1 (case 1).—Ventriculograms.

A, anteroposterior view, showing decreased filling of the right lateral ventricle with depression of the posterior portion of the body (indicated by arrow).

B, right lateral view. The depression of the posterior part of the ventricular body is shown by the arrows. This might well be considered a normal variant of the ventricle.

to the left side: They consisted of slight impairment of pain and temperature senses over the distribution of the trigeminal nerve (including a decreased corneal reflex) and downward to the fifth thoracic segment, moderate impairment of pain and temperature senses from the fifth to the tenth thoracic segment and complete loss of pain and temperature senses below the tenth thoracic segment. Position and touch senses were preserved bilaterally.

Consultation with the department of ophthalmology on July 23 showed that the patient's vision was 20/70 in the right eye and 20/60 in the left eye, without correction. There was crossed diplopia to the right,

indicating weakness of the left internal rectus muscle. The conjunctiva was normal. The disks showed choking of approximately 5 D. bilaterally. Veins were engorged over the disks but not excessively so in the surrounding fundi. There were a few scattered hemorrhages. The visual fields were full, with greatly enlarged blindspots. The impression was that there was an intracranial mass lesion with resulting choked disks. (Ophthalmoscopic examination on July 10 had shown papilledema, of 3 D. in the right eye and of 2 D. in the left eye.)

Medical consultation was obtained. It was the opinion of the consultant that while the patient had polycythemia this condition probably did not account for the high degree of choked disk or the bizarre neurologic findings. Turpentine fumes, to which the patient had been exposed for a number of years, were suggested as a possible cause of the polycythemia.

Because of the progression of symptoms, a ventriculographic examination was done under local anesthesia, on July 27. The occipital approach was used. Twenty cubic centimeters of clear fluid was obtained from the left lateral ventricle and 15 cc. from the right lateral ventricle. Dye passed readily between the two lateral ventricles. There was no ventricular shift, the only deviation from normal being apparent failure of the right lateral ventricle to fill as well as the left, with a questionable depression of the posterior part of the body of the right lateral ventricle (fig. 1). However, the change was so slight that it did not justify a diagnosis of tumor.

On August 2, 3 and 5, 500 cc. of blood was withdrawn by venipuncture. The results are seen in table 1. There was no apparent clinical improvement. Indeed, on August 15, visual acuity was 20/100 in the right eye and 20/70 in the left. Papilledema had increased to 6 D. bilaterally, and the visual fields showed definite suggestion of a left homonymous field cut (fig. 2*A*).

After further review of the case, a craniotomy was done in the right frontotemporal region on August 18 for exploration and decompression, in an effort to preserve vision. When the bone flap was turned back, the dura was found to be light green. As the dura was opened, the neomembrane characteristic of chronic subdural hemorrhage appeared (fig. 3). The dura was further opened, and 15 to 20 cc. of coffee-colored fluid escaped. The rest of the clot, which was about 1 cm. thick and covered the posterior parietal area, was evacuated without difficulty. The region of the optic nerve was explored, only a few fine adhesions being found. A wide decompression was provided at the base of the flap; the dura was cut free, turned over and sutured into place. The bone flap was replaced and wired. A drain was inserted through a posterior stab wound, and the galea and skin were sutured with black silk. A trephine opening was made over the left parietal area, no evidence of hemorrhage being found. The postoperative course was completely uneventful.

On August 29, her visual acuity was 20/70 in the right eye and 20/60 in the left. Diplopia had disappeared, and the papilledema measured 4 D. on the right side and 3 D. on the left side. The visual fields

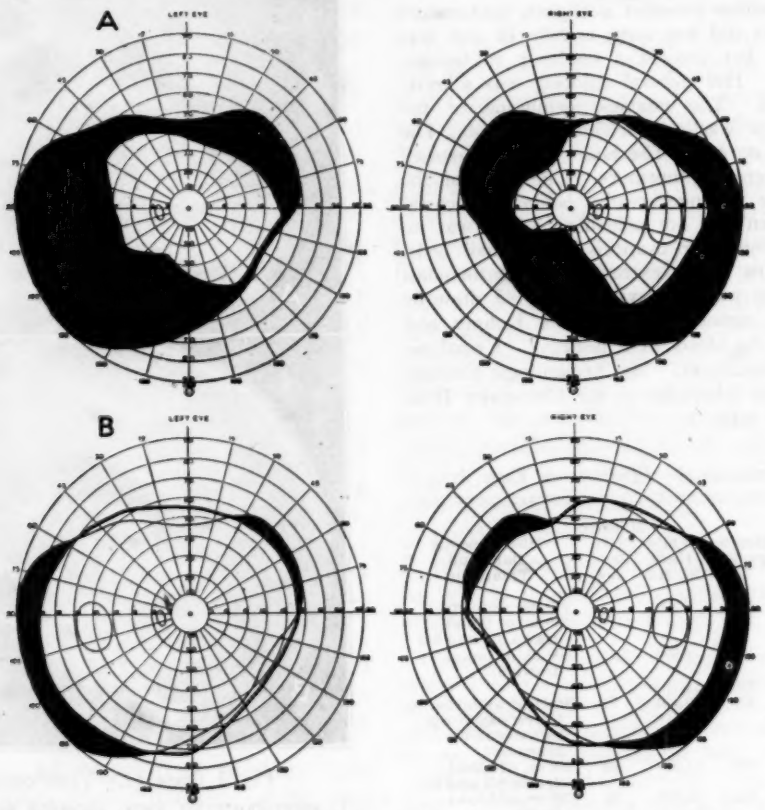

Fig. 2 (case 1).—Visual fields. *A*, fields before operation, showing generalized peripheral contraction with suggestive left incongruous homonymous hemianopsia.
B, fields after removal of subdural hematoma, showing normal peripheral vision.

showed notable improvement, with filling in of the defects noted in the previous examination.

The patient was discharged on September 12, with her condition much improved.

On September 22, her eyegrounds showed papilledema of less than 2 D. There was some fulness at the site of the decompression. She was last seen Jan. 22, 1945. The site of her decompression was soft but slightly tender. She had gained 10 pounds (4.5 Kg.) in weight and felt much better. She said her left leg and foot were still numb. Physical examination revealed nothing significant. Sensory examination revealed normal sensation for all modalities downward to the level of the tenth thoracic segment; there was moderate decrease of pain and temperature sensations to the level of the greater trochanter on the left side. Below this level, there was loss of pain and temperature sensations on the left side. Touch and position senses were preserved. There was slight weakness of the left lower extremity. The reflexes were physiologic.

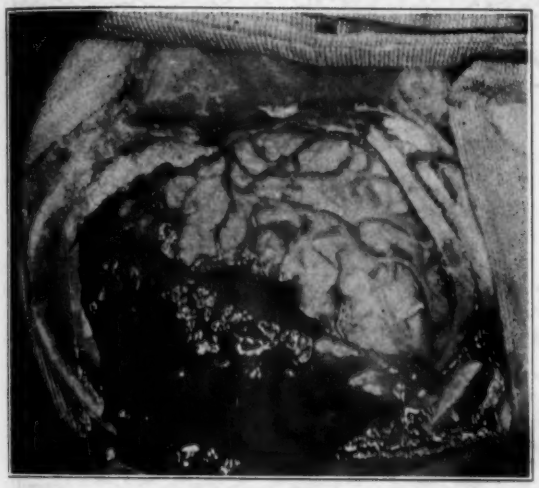

Fig. 3 (case 1).—Operative field. The large, chronic subdural hematoma is seen overlying the superior portion of the right parietal cortex. The temporal muscle, acting as a hinge for the bone flap, is at the top of the picture.

Ophthalmoscopic examination showed the nasal margin of the right disk to be blurred; the margin of the left disk was blurred throughout. There was questionable papilledema of 0.5 to 1 D. in each eye. The veins were not engorged, and the retina appeared normal. Visual acuity was 20/70 in the right eye and 20/100 in the left eye, without correction. With the pinhole disk it became 20/40 and 20/60, respectively. The visual fields were full; the blindspots were not enlarged (fig. 2 *B*). Hematologic studies, the results of which are shown in table 1, indicated a beginning return of the polycythemia.

Pathologic Study.—The specimens removed at operation consisted of organized blood clot and membrane. Microscopically, the membrane consisted of fibrous tissue filled with small vascular channels, which were filled with red blood cells. It also contained many large mononuclear cells with homogeneously stained blue nuclei. The fibrous elements were mostly reticulin, with some collagenous fibers. Also, some fairly fresh blood clots were present. A small portion of the membrane had a better organized appearance and contained more fibroblastic cells, with fewer infiltrating blood cells. The diagnosis was membrane of a chronic subdural hematoma with cellular infiltration (fig. 4).

That this case was confusing is evident. The neurologic findings, the polycythemia, the papilledema and the normal ventriculogram all combined to make it extremely difficult to know what course to pursue. An operation was finally performed in an effort to preserve the patient's vision. The fact that a chronic subdural hematoma was found and removed, with notable improvement in the patient's symptoms, serves further to cloud the issue, since it is impossible to say whether the hematoma was caused by the minor head injury sustained in February, whether it was the result of hemorrhage due to polycythemia or whether it was the cause of the polycythemia. That it might be the result of hemorrhage from the polycythemia is suggested by the presence of fresh blood clots in the microscopic sections of the membrane. It is also of interest to note that the red blood cell count, which was somewhat low before operation, probably as the result of bleeding, fell notably after operation and remained low for approximately five months. This, again, suggests a possible relationship between the central nervous system and polycythemia.

In 1943, Tinney, Hall and Giffin [4h] reviewed the cases of 163 patients with polycythemia. Of these, 127 had signs referable to the central nervous system. In 2 of these "a cerebral neoplasm was actually found present." No further details are given. In this series, a tumor of the brain was suspected in only 8 cases. Galíndez and Sanguinetti [10] reported a case in which an "endothelioma" was found in the right frontal region at autopsy. The patient had weakness of the left arm and leg, bilateral papilledema (marked), a cerebrospinal fluid pressure of 500 mm. of water, a red blood cell count of 8,920,000 and a hemoglobin concentration of 125 per cent. Studies of the blood and bone marrow confirmed the case as one of polycythemia vera. With the case reported by us, there is a total of 10 reported cases in which an expanding intracranial mass lesion, not of the diencephalic area, was associated with polycythemia. No case has previously been reported in which chronic subdural hematoma was found with polycythemia.

The actual cause and effect relationship between lesions of the brain and polycythemia has never been definitely established, although the

10. Galíndez, L. V., and Sanguinetti, L.: Polyglobulia Vera with Right Frontal Tumor: Clinical and Anatomico-Pathologic Study of a Case, Rev. méd. latino-am. **19**:1055-1072 (July) 1934.

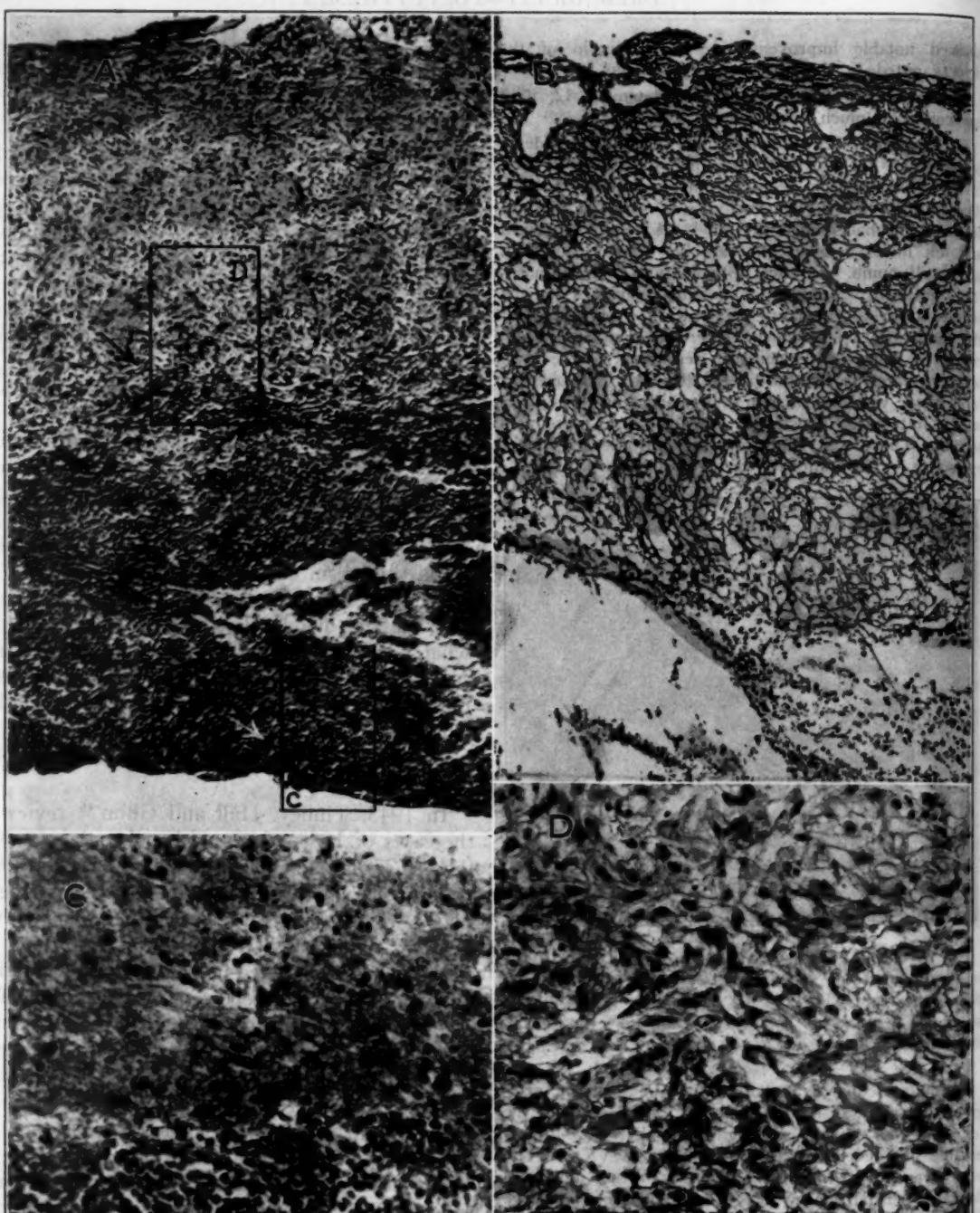

Figure 4

(See legends on opposite page)

feeling that it probably exists has been noted by a number of writers.[11] Other authors have stated that on the basis of clinical studies alone one must accept it as a distinct factor.[12] Carpenter, Schwartz and Walker,[5] in the conclusion of their paper, stated with regard to the polycythemia in their 2 cases: "We believe it to be of neurogenic origin." Excellent reviews on this phase of the subject are provided by several authors.[13] The experimental work done on animals [6g] is certainly suggestive but is not of sufficient volume to be conclusive at this time.

PAPILLEDEMA AND POLYCYTHEMIA

The fundus picture which occurs with polycythemia is of particular interest in the effort to establish a differential factor for distinguishing between an intracranial mass and polycythemia as the cause of a given set of symptoms. This picture, which in the typical case is called "fundus polycythemicus," is well recognized and quite characteristic. It has been described in considerable detail by many writers, including de Schweinitz and Woods.[14]

> The usual fundus picture of polycythemia, if there is a characteristic fundus picture, consists of dilatation, sometimes uneven, of retinal veins, and deepening of their color, and alterations, cyanotic in type, of the normal color of the eyegrounds, without hemorrhages, or exudates or changes in the optic nerve, and generally without marked change in the caliber of the arteries.

These authors also noted that blurring of the margins of the disks may often occur. Venous dilatation becomes pronounced when the hemoglobin concentration is 110 per cent or more, and retinal cyanosis occurs only when the hemoglobin content exceeds 125 per cent. Weber [15] also discussed this picture in considerable detail. In all the 13 cases at this hospital in which the presence of severe neurologic signs was previously mentioned, full purplish veins were noted; in 5 the margins of the disks were pathologically blurred, and in 1 the disk was almost obliterated by hemorrhages. In another case, in which the patient died one week after admission and in which cerebellar impaction was found at autopsy, there was only venous distention. Papilledema was not noted in any case.

In 1929, Brockbank [4b] reviewed 56 cases of polycythemia, in only 1 of which papilledema was present but in all of which definite neurologic damage existed. Adams [4a] reviewed 9 cases "with special reference to nervous manifestations" and did not mention papilledema as occurring in any. Dameshek and Henstell [16] and Fucher [4d] gave excellent discussions of polycythemia as a general medical problem but did not bring choked disk into the picture. On the other hand, Weber [15] stated:

> Probably the ophthalmoscopic changes of "cyanosis retinae" may progress to choked disc and typical optic neuritis, not only in ("primary") erythremia, but in cases of chronic cyanosis with secondary polycythemia when of cardio-vascular origin.

Duke-Elder [17] stated that there may be "oedema of the disc, which may even simulate papilledema due to cerebral tumour." With these statements in mind, we felt that a review of the existing literature, with the addition of a case of our own, would be worth while.

CASE 2.—E. C., a 49 year old white laborer, was admitted to the neurosurgical service of the Hospital of the University of Pennsylvania on Oct. 23, 1940, complaining of loss of vision, diplopia and chronic headache.

The patient, a chronic alcoholic addict, had been in his usual state of health until August 1940, when he began to suffer from generalized headaches, which became progressively more frequent and severe until finally they became constant. Two weeks after the onset of headaches, he noticed beginning failure of vision. This was followed by diplopia, which became more pronounced. His vision on admission was so poor that he was unable to read a newspaper. He had been slightly deaf in the right ear since 1930.

11. Baserga.[6a] Guillain, Lechelle and Garcin.[6f] Salus.[6g]

12. Castex,[6c] Da Rin and Costa.[6d] Ferraro and Sherwood.[6e]

13. Carpenter, Schwartz and Walker.[5] Castex.[6c] Da Rin and Costa.[6d] Ferraro and Sherwood.[6e]

14. de Schweinitz, G. E., and Woods, A. C.: Concerning the Ocular Symptoms of Erythremia (Chronic Polycythemia Vera) with Special Reference to the Fundus Picture, Tr. Am. Ophth. Soc. **23**:90-105, 1925.

15. Weber, F. P.: Polycythemia, Erythrocytosis, and Erythremia, London, H. K. Lewis & Co., Ltd., 1921, p. 82.

16. Dameshek, W., and Henstell, H. H.: The Diagnosis of Polycythemia, Ann. Int. Med. **13**:1360-1388 (Feb.) 1940.

17. Duke-Elder, W. S.: Text-Book of Ophthalmology, St. Louis, C. V. Mosby Company, 1941, vol. 3, pp. 2738-2739.

EXPLANATIONS OF FIGURE 4

Fig. 4 (case 1).—Membrane of chronic subdural hematoma. *A*, low power, showing fibrous outer membrane overlying organizing blood clot, which contained many fresh red blood cells (arrows). Hematoxylin and eosin stain; × 75. *B*, outer membrane, showing fibrous structure. Wilder stain; × 150. *C*, margin of hemorrhagic layer, with large mass of fresh red blood cells in the midst of the older clot. Hematoxylin and eosin stain; × 330. *D*, junction of the fibrous and the hemorrhagic layer, showing mass of fresh red blood cells. Hematoxylin and eosin stain; × 280.

About Sept. 10, 1940, he first noticed tinnitus in both ears. He had lost considerable weight (exact amount not known) and was "run down."

Physical examination showed that the patient was emaciated but not acutely ill. His skin was warm and dry and had a ruddy, cyanotic color. The left eye was slightly more prominent than the right. There was moderate conjunctival congestion. Hearing was grossly impaired in the right ear, bone conduction being greater than air conduction, with sound localized to the right in the Weber test. The mucous membrane of the mouth and pharynx was not injected or cyanotic. The lungs had occasional, scattered rales throughout. The heart was not enlarged; there was an apical systolic murmur. The liver was questionably palpable on deep inspiration; the spleen was not palpable. The extremities showed emaciation but no localized weakness. The blood pressure was 136 systolic and 88 diastolic when the patient was in the supine position. Urinalysis revealed nothing abnormal. The Kolmer and Kahn reactions of the blood were negative; the plasma protein measured 6.9 Gm. per hundred cubic centimeters, and the chlorides, 97.7 milliequivalents. The hematologic findings are listed in table 2.

TABLE 2.—*Hematologic Findings in Case 2*

Date	Red Cells (Cu. Mm.)	Hemoglobin, %	White Cells (Cu. Mm.)	Miscellaneous Data and Treatment
10/24/40	8,880,000	140	10,800	Hematocrit reading, 72; volume index, 0.88
11/ 6/40	8,250,000	134	7,500	
11/ 7/40	9,080,000	144	12,400	
11/11/40	7,400,000	136	12,000	1,000 cc. of blood drawn
11/13/40	8,100,000	118	11,100	Hematocrit reading, 64; volume index, 0.80
11/18/40	Right frontoparietal craniotomy			Transfusion of 1,000 cc. of blood
11/21/40	4,400,000	76*	17,000	
11/27/40	3,800,000	73	9,700	
12/ 2/40	4,500,000	75	18,300	Patient discharged 12/20
3/12/41	5,000,000	96	.....	
6/13/41	.....	105	.....	
9/16/41	7,900,000	116	8,200	

Lumbar puncture revealed that the fluid was xanthochromic and the pressure 510 mm. of water. There were 130 red blood cells and 30 white blood cells (20 polymorphonuclear leukocytes, 10 mononuclear cells) per cubic millimeter. The protein measured 50 mg. per hundred cubic centimeters. The serologic reactions were negative; the colloidal gold curve was 0000000000. Roentgenograms of the chest and skull were normal.

Neurologic examination showed the motor and sensory systems to be intact. There were horizontal nystagmoid movements to the right and to the left and pronounced bilateral papilledema with hemorrhages. The reflexes were physiologic. There was some tremor on both sides on performance of the finger to nose test.

The patient was seen in consultation by members of the medical service, and their feeling was that all his symptoms might be accounted for on the basis of his polycythemia. Phlebotomy was suggested as a means of preventing further progression of the process. One thousand cubic centimeters of blood was withdrawn, without change in his symptoms.

Because of his visual complaints and the obvious pathologic condition in his eyes, the department of ophthalmology was asked to see the patient, on October 24. Visual acuity was 10/200 in the right eye and 20/200 in the left eye. The external examination revealed an essential normal condition. The ophthalmoscopic examination showed that the right disk was elevated 7 D., the papilledema being of the collar button type, with encroachment on the macular area. There were few macular bands; no star-shaped figure was present. The veins were engorged, and there were a few scattered hemorrhages and exudates about the nerve head. The peripheral portion of the retina was normal. The left eye was similar to the right except that the papilledema measured 5 D. Both central visual fields showed enlarged blindspots. The papilledema gradually decreased until, on Nov. 4, 1940, it was only 4 D. in each eye and was more diffuse. On November 11, two days after the withdrawal of 1,000 cc. of blood, the right eye showed 3 D. of choking with many hemorrhages, and the left eye, 4.5 D. of choking with hemorrhages around the disk.

Opinion was divided as to whether the signs and symptoms were due to polycythemia or to an intracranial mass, the immediate problem being the preservation of vision. The papilledema did not decrease after the initial change; because of this, it was decided that at least a decompression should be done to relieve the increased intracranial pressure.

On November 18, under local anesthesia, the lateral ventricles were tapped by the occipital route, and considerable pressure was encountered. The left lateral ventricle contained 35 cc. of fluid; the right lateral ventricle contained only 3 to 4 cc. In view of these findings and the absence of localizing neurologic signs, the possibility of a tumor in the right frontal lobe was considered and a craniotomy in the right frontoparietal region was immediately done, under local anesthesia.

When the bone flap was turned back, the dura, rather than being tense, as might have been expected from the pressure found when the ventricles were tapped, was notably relaxed. It was opened from below upward, revealing marked cortical atrophy. The sulci were full of fluid, and the surface of the cortex was covered with a semiopaque membrane. This was incised and considerable clear fluid allowed to drain out, thus accentuating the atrophy of the cortex. There was obviously no tumor present; so the dura was free grafted, sutured and drawn up to the bone, after all bleeding points had been secured. The dura was left open at the base to provide a wide decompression. The bone was replaced and wired, and the galea and skin were closed with black silk, without drainage

After operation the patient received phenobarbital, ½ grain (0.032 Gm.), to forestall possible convulsions. He was drowsy; so this medication was discontinued on November 24. On November 25 weakness developed on the left side, which became paralysis on the following day. On November 27, he had a clonic convulsion of the left arm and leg. He was once more given phenobarbital, and no more convulsive attacks occurred. On November 29, he was moved into a wheel chair, and from then on his convalescence was smooth.

The ophthalmologic examination, sixteen days after operation, showed, on the right, beginning optic nerve atrophy and 4 D. of papilledema. The fundus was much paler than before operation, and the veins were thinner and not dark or engorged. There were a few scattered hemorrhages. On the left the papilledema was 3 D., the rest of the picture being similar to that seen on the right. The impression at this time was retinal anemia, bilateral papilledema and secondary optic nerve atrophy.

The patient was discharged on Dec. 20, 1940, with instruction to return to the outpatient department.

On March 21, 1941, he was again seen. The red blood cell count was 5,000,000, and the hemoglobin concentration, 96 per cent. There was no vision in the right eye. Vision in the left eye was 20/80, with a full peripheral field. Subjectively, he was much better. On June 16, 1941, he showed considerable improvement. Vision was 20/40 in the left eye and was limited to perception of fingers at 5 feet (152 cm.) in the right eye. Perimetric examination showed a full visual field on the left and moderate contraction on the right (fig. 5). No measurable papilledema was present. There was bilateral secondary optic nerve atrophy. The hemoglobin concentration was 105 per cent. Neurologic examination failed to show any residual weakness on the left side. On Sept. 10, 1941, he returned, complaining of "loss of pep." Vision was unchanged. There was bilateral optic nerve atrophy, with choking of 1 to 2 D. on the right side and 1.5 to 2 D. on the left side. The reflexes were hyperactive. No pathologic reflexes were present. The red blood cell count was 7,900,000; the hemoglobin content, 116 per cent. The patient died at his home Jan. 17, 1942; no further details were available.

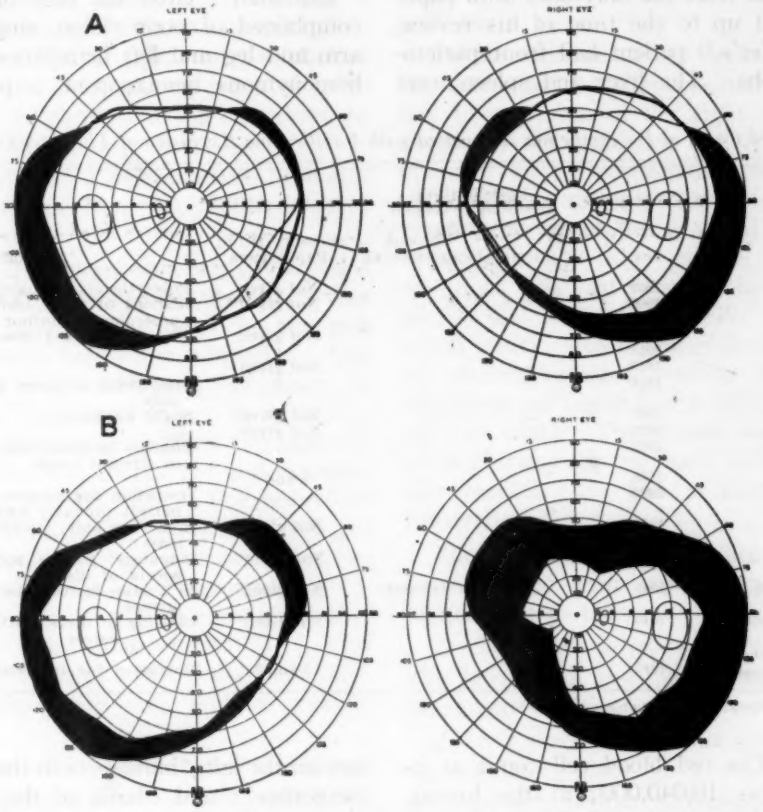

Fig. 5 (case 2).—Visual fields. *A*, before operation. The central fields showed notable enlargement of the blindspots. *B*, after operation. The right field was definitely contracted. Visual acuity, however, was improved, especially in the left eye.

Diagnostically, this case presented a real problem. It was the opinion of members of the medical department that all symptoms could be accounted for on the basis of polycythemia. On the other hand, the ophthalmologists expressed the belief that the papilledema was of too great a degree to be compatible with such an explanation. In the meantime, though the papilledema became less pronounced, vision did not improve, and optic nerve atrophy began to develop. The neurosurgical service, faced with these conflicting opinions and facts, felt that the least that could be attempted was a decompression, in an effort to preserve as much vision as possible. This was done, with negative results as far as finding a tumor was concerned and with indifferent results from the standpoint of preserving vision. It is extremely interesting to note that immediately after operation, and for eight months thereafter, the hemoglobin level stayed within or below normal limits. Only three months before the patient's death did it begin to rise.

As far as we are able to determine, a total of 17 cases of polycythemia have been reported in which the optic disks showed changes which may be considered as papilledema or choked disk (exclusive of cases in which polycythemia was associated with an expanding intracranial mass). This review includes Knapp's [18] case, described

18. Knapp: A Case of Hyperemia of the Retina with Choked Disc, Verhandl. d. naturh.-med. Ver. zu Heidelberg **2**:84-86, 1859-1862.

before polycythemia was recognized, which Kümmel [19] believed to be one of polycythemia.

Russell,[20] in 1906, reported "a case of cyanosis with polycythemia" in which the red blood cell count was as high as 8,650,000 (hemoglobin, 120 per cent) and the disks showed "considerable blurring of the edges, obviously due to edema." Whether the "blurring" and "edema" were of the type considered now to be a relatively frequent finding in the polycythemic fundus, or whether there was true papilledema, is open to question. Lucas [4f] evidently felt they were not significant, since he flatly stated that his and Pfeiffer's [21] cases were the only ones with papilledema reported up to the time of his review, in 1912. Pfeiffer's [21] patient had frontoparietooccipital headache. The liver and spleen were bilateral choking of 2 D. Lucas [4f] reviewed 189 reported cases of polycythemia and added 2 of his own. In his first case there was concentric contraction of the visual fields, with 4 D. of papilledema bilaterally. The report on the eyegrounds stated that the "changes are those of typical inflammatory choked disk, identical, it would seem, with those frequently seen with intracranial disturbance." The patient complained of headache and blurred vision. The red blood cell count ranged from 5,200,000 (hemoglobin, 96 per cent), after bleeding, to 8,660,000 (hemoglobin, 140 per cent), before bleeding.

Christian [4c] cited the case of a patient who complained of poor vision, tingling in the left arm and leg and left hemiparesis. He had left homonymous hemianopsia, a positive Babinski

TABLE 3.—*Reported Cases of Polycythemia Associated with Papilledema Exclusive of Those with Intracranial Mass**

Author(s)	Year	Classification According to Author: Edema	Classification According to Author: Choking (Papilledema)	Amount (D.) of Papilledema	Comment
Knapp	1859	..	+	Not given	Polycythemia probably present
Russell	1906	+	..	Not given	Blurring of edges, obviously due to edema, according to author
Pfeiffer	1907	..	+	Not given	Moderate choked disk
Lucas	1912	..	+	4	
Christian	1917	+	..	Not given	
Cohen	1918	..	+	3	Papilledema of nasal margin of left papilla only
Redlich	1920	..	+	Not given	Slight choking
Nueda	1922	..	+	Not given	
Moore	1922	..	..	.....	Changes in disks little different from those of cerebral tumor
Horder	1926	..	+	2 and 5	
Oppenheimer	1929	..	..	.....	Operation for suspected brain tumor; patient probably had papilledema
Brockbank	1929	..	+	Not given	Right eye only; operation for intracranial mass
Cohen	1937	+	..	Not given	Diagnosis: fundus polycythemicus with edema of disk
Tinney, Hall and Giffin	1943	..	+ (4 cases)	Not given	In 2 cases intracranial mass probably present
Lowman, L., and Dameshek, W.: New England J. Med. 232 : 394-397 (April 5) 1945	1945	..	+	Not given	Choking of disks, particularly over nasal halves
Drew and Grant	1945	..	+	5 and 7	Operation for suspected brain tumor

* For 2 possible exceptions see table.

not enlarged. The red blood cell count at its highest point was 10,040,000; at the lowest, 5,968,400. The hemoglobin values ranged from 155 to 100 per cent. The eyegrounds showed "moderate" choked disks with vague margins. The cerebrospinal fluid pressure on lumbar puncture was 370 mm. of water. In this same case, as reported later by Behr,[22] there was sign on the left, "blindspots in the field of vision" (scotomas?) and edema of the disks (amount not stated). For ten years it had been suspected that he had a tumor of the brain. A "cerebral decompression" was done. He subsequently died. Autopsy showed bilateral thrombosis of cerebral arteries with cortical degeneration.

Cohen,[23] in 1918, reported a case in which there was a two year history of failing vision in the right eye and hot flushes. There were plethora, cyanosis and enlargement of the liver and spleen. The red blood cell count ranged from 8,000,000 to 10,000,000, and the hemoglobin level, from 140 to 160 per cent. The Wassermann reaction of the blood was strongly

19. Kümmel, U., in Schieck, F., and Brückner, A.: Kurzes Handbuch der Ophthalmologie, Berlin, Julius Springer, 1931, vol. 7, p. 74.

20. Russell, J. W.: A Case of Cyanosis with Polycythemia, Lancet **2**:20-21 (July 7) 1906.

21. Pfeiffer, W.: A Case of Polycythemia Without Splenomegaly, Deutsches Arch. f. klin. Med. **90**:609-617 (July) 1907.

22. Behr, C.: The Nature of the Ocular Changes in Polycythemia Together with a Contribution on the Theory of Choked Disc, Klin. Monatsbl. f. Augenh. **48**:672-688, 1911.

23. Cohen, M.: Eye Manifestations in a Case of Polycythemia, Arch. Ophth. **47**:192-194 (March) 1918

positive. Examination two years previous to the patient's admission showed a typical fundus polycythemicus. On admission, the patient had no vision in the right eye, and the nasal margin of the right papilla was blurred. The left disk was yellowish white on the temporal side, with a sharp outline. The nasal margin showed papilledema of 3 D.

A case of erythremia with a red blood cell count of 7,200,000 (hemoglobin, 115 per cent), enlarged spleen and liver, cyanosis and "slightly" choked disks was reported by Redlich.[24]

Nueda [25] reported a case in which were present cyanosis, enlarged spleen and liver and a red blood cell count of 7,000,000 to 8,000,000. He particularly called attention to the choked disk, which he said was rare in cases of polycythemia. The cerebrospinal fluid pressure in this case was 300 mm. of water.

Moore [26] mentioned a case in which "the disc changes differed little from the papilloedema ot a cerebral tumor."

Seven cases of polycythemia with neurologic complications were discussed by Horder.[4e] One of the patients (case 4) had headache and stiff neck fifteen months before her admission. She also complained of blurred vision and occasional diplopia. Nine months previous to admission she noticed impaired sense of smell and intervals of blindness. She was cherry red and cyanotic. The spleen was not palpable. The red blood cell count was 6,320,000 (hemoglobin, 100 per cent). The hemoglobin level eventually reached 134 per cent. Notes on the eyegrounds stated: "The disc edges are greatly obscured; the discs themselves are swollen about 2-5 D." Five months later the changes in the disks were indistinguishable from those seen with a cerebral neoplasm.

The 1 patient whom Brockbank [4b] mentioned as having papilledema came to him with a history of having had choked disk in the right eye two years previously, although none was present at the time of Brockbank's examination. The patient had sustained a previous head injury, after which he had failing vision. Chronic polycythemia developed four months after the accident, the red blood cell count being 6,400,000 (hemoglobin, 108 per cent). On the basis of the visual changes and the results of ventriculographic studies, operation for a suspected intracranial lesion was carried out, but nothing was found. Cohen,[27] in 1937, reviewed 7 cases of polycythemia and discussed the ophthalmic findings. In 1 of these (case 5) there was a red blood cell count of 7,800,000 (hemoglobin, 140 per cent) and "edema" of the disk—the amount not being given.

Tinney, Hall and Giffin,[4h] in their review previously mentioned, reported choked disks in 4 of 163 cases. The amount of choking was not stated, nor was it indicated whether these 4 cases included the 2 mentioned earlier as instances of cerebral tumor, although this is probable.

To the aforementioned series may be added the case cited by Oppenheimer.[8] The patient had paresthesias on the right side with hemiparesis of the same side and aphasia. He was operated on for suspected tumor of the brain, with negative results. There is no mention of papilledema or of the eventual outcome of the case. The only other case in which operation was done was that reported by Adams.[4a] The patient had fainting spells and convulsions after a bad injury. Roentgenograms of the skull and air studies revealed nothing significant. The red blood cell count was 9,500,000 (hemoglobin, 145 per cent). The patient was later operated on in Norway for traumatic epilepsy, with negative results. He had a severe postoperative hemorrhage.

The 19 cases of polycythemia presumed to be associated with papilledema (table 3) may be analyzed as follows:

1. One case was reported before polycythemia was recognized, and the diagnosis must be on a presumptive basis.

2. In 2 cases papilledema may be assumed to have existed, since in 1 case ocular changes were present similar to those found with brain tumor and in the other operation for suspected cerebral tumor was performed.

3. In 2 cases papilledema was noted in only one eye, and in 1 of these on only the nasal margin of the disk.

4. In 3 cases the changes were referred to as "edema of the disk," rather than as choking or papilledema.

5. In 13 cases choking or papilledema occurred as such, but in 2 of these there was probably an associated tumor of the brain.

6. Of the 13 cases, the amount of papilledema was stated in only 4, the range being 2 to 7 D.

24. Redlich, F.: Erythremia (Polyglobulia) and Erythromelalgia, Wien. med. Wchnschr. **70**:959-962 (May 15) 1920.

25. Nueda, P.: A Case of Erythremia (Vaquez) with Erythromelalgia with Choked Disc, Wien. med. Wchnschr. **72**:533 (March 18) 1922.

26. Moore, R. F.: Medical Ophthalmology, ed. 1, London, J. & A. Churchill, 1922, p. 82.

27. Cohen, M.: Lesion of the Fundus in Polycythemia Arch. Ophth. **17**:811-818 (May) 1937.

7. In 3 cases operation was performed for a suspected intracranial mass lesion, with negative results.

From those facts, it is evident that while papilledema can and does occur in association with, and as the result of, polycythemia, it is not a common finding, and, indeed, may be considered as an unusual complication. Because of the tendency for signs and symptoms referable to the central nervous system to develop with this disease, the association of papilledema with these changes may present a real and serious neurosurgical problem. If intracranial disease, including expanding mass lesions, is further considered as a possible cause of polycythemia, one is confronted with something more than the usual questions involving diagnosis and treatment. There is a growing volume of literature in support of the latter relationship, and the neurosurgeon must be prepared to recognize and cope with situations of this type.

SUMMARY AND CONCLUSIONS

The importance of polycythemia as a differential problem in neurosurgery is real. Complications referable to the central nervous system in cases of polycythemia are extremely frequent, and recognition is accorded the growing number of such cases. In the first case presented, chronic subdural hematoma was associated with polycythemia, which disappeared after removal of the hematoma but showed a tendency to return five months after operation. A review of the literature concerned with the coincident occurrence of expanding intracranial mass lesions and polycythemia revealed 9 cases in which the diencephalic region was not involved. A brief discussion of the "usual" fundus picture of polycythemia is given. In the second case presented, papilledema of high degree was associated with polycythemia, and the existing literature on this relationship is reviewed.

It may be concluded that the occurrence of a true expanding intracranial mass lesion with polycythemia is rare but that the coincident occurrence of papilledema and polycythemia is somewhat more common. However, this association is not as frequent as might be suspected from casual comments in the literature. The cause and effect relationship between polycythemia and disease of central nervous system is becoming increasingly well documented, but the volume of work done is not yet sufficient to warrant its being recognized as an established fact.

Polycythemia with papilledema must be considered as a possible diagnostic and operative problem for the neurosurgeon.

HYPOTHALAMIC ATTACKS WITH THALAMIC LESION

I. PHYSIOLOGIC AND PSYCHOLOGIC CONSIDERATIONS

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The functions of the hypothalamus have been elucidated by the careful studies of Bard, Fulton, Long, Masserman, Ranson, Sheehan and their co-workers on animals.[1] Observations on patients with structural lesions of the hypothalamus have amply confirmed these studies. Most of the clinical examples, however, have been concerned with destructive lesions of some portion of the hypothalamus and, consequently, with more or less static disturbances of function, such as diabetes insipidus, hyperthermia and hypothermia, etc. More unusual have been cases in which periodic massive discharges of hypothalamic activity have taken place, such as the case of a ball valve tumor of the third ventricle reported by Penfield.[2]

To our knowledge, there is no report of a destructive and fixed lesion outside the hypothalamus leading to disturbance of hypothalamic function with repeated display of exaggerated hypothalamic activity. The present case represents such an example; a cystic, degenerative lesion involving chiefly the dorsomedial and lateral nuclei of the right thalamus, apparently acquired at birth, was associated with repeated paroxysms of hypothalamic overactivity, the final attack terminating in death in the eighteenth year. The location of this small lesion was such as probably to interrupt some corticohypothalamic association fibers. The hypothalamus itself was intact.

The minute neuroanatomic lesion was in itself not sufficient to explain the clinical picture. An adequate understanding of the dynamics of the case became possible only after proper consideration of certain essential physiologic and psychologic factors.

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1. (*a*) Fulton, J. F.: Physiology of the Nervous System, ed. 2, New York, Oxford University Press, 1943, p. 614. (*b*) The Hypothalamus, Proceedings of the Association for Research in Nervous and Mental Diseases, Baltimore, Williams & Wilkins Company, 1940, vol. 20.

2. Penfield, W. G.: Diencephalic Autonomic Epilepsy, Arch. Neurol. & Psychiat. **22**:358-374 (Aug.) 1929.

PHYSIOPATHOLOGIC STUDY

The patient was a white youth 17¾ years of age at the time of his death. He had been born prematurely and weighed 5 pounds 5 ounces (2,410 Gm.) at birth. Birth was uneventful, and at delivery the infant appeared to be in good condition. The pregnancy had been normal except that the mother suffered from repeated urticaria during the early months of gestation. Copious administration of epinephrine resulted in symptomatic relief.

On the third day of life the infant had a "blue spell." This marked the first of a series of different types of episodes which occurred repeatedly throughout his life. Until the age of 13 the boy experienced numerous spells in which he was said to hold his breath, become cyanotic and lose consciousness. It is estimated that he had between 125 and 150 of these spells, which occurred less frequently in later years, and not after the age of 12 years. Occasionally he would have them during his sleep. It was thought that the attacks were precipitated by crossing the child, and he was known to have them on passing a cemetery, which he did not like to enter. Abandoned laughter precipitated attacks. In these episodes his head would be thrown backward, and he would lapse into unconsciousness. The extremities would extend and the hands pronate. He was not incontinent. An attack would last less than a minute and was followed by deep sleep. He never had a clonic convulsion. Because of the episodes of "breath holding," the thymus gland was examined roentgenographically in infancy and was found to be enlarged. He was given an occasional irradiation over the thymus, the last at the age of 5 or 6 years, when he had received a total of twenty treatments.

At the age of 5 months a second type of attack had its inception, the final one of which was associated with his death. Over the course of the years there had occurred 15 to 20 of these episodes. All the attacks followed essentially the same pattern, although they differed somewhat in intensity and duration. The attack was usually ushered in by what appeared to be rhinitis. With the onset of the attack he complained of coldness, shivered and sometimes had a chill. The face and extremities were noted to be cold and pale, while the trunk was warm. Sweating was absent in this phase. The presence or absence of piloerection was not noted in any of the records. During this period the rectal temperature rose rather abruptly in the course of a few hours to 105 or 106 F. The pulse was rapid, while the blood pressure, though fluctuating between moderate hypertension and hypotension, usually tended to fall. The patient appeared critically ill in this phase. Rales were heard in the chest. The rectal temperature usually remained elevated several hours and then would suddenly fall. The sudden defervescence was marked by profuse sweating and flushing of the trunk and extremities. Rapid swings of temperature then occurred for the next three to four days, the temperature tending toward nor-

mal with the passage of time. It was unusual to find the temperature the same on any two successive readings, taken as frequently as one-half to one hour apart, and he sometimes had a number of spikes daily. Later it was found that the attacks and fever could be aborted by pentobarbital sodium, as well as by the usual antipyretics.

All the attacks were accompanied with evidence of pronounced gastrointestinal overactivity. The patient experienced severe cramps, nausea and vomiting and was unable to retain food for several days. Occasionally the vomitus contained blood. Sometimes the vomiting persisted longer than the disturbances in temperature and once lasted ten days. Diarrhea also accompanied some of the attacks.

During the attacks there was usually oliguria; the urine was concentrated and contained albumin and hyaline and granular casts. Evidences of hemoconcentration were present. The blood urea nitrogen rose, on one occasion reaching 88 mg. per hundred cubic centimeters. With recovery, the urine rapidly returned to normal except for the presence of casts, which persisted until the age of 13 and then disappeared, to reappear with the feverish attacks. In routine urinalyses the specific gravity ranged from 1.010 to 1.025. The white cell count was usually normal during an attack. All the episodes were associated with severe cramplike pains in the arms and legs. It was thought that these might have been related to the excessive vomiting.

With each attack he lost 8 to 10 pounds (3.6 to 4.5 Kg.) but regained this weight quickly. The attacks were terminated by the unexpected announcement that he again felt well.

His family, which included an intelligent, observant physician (his father), noted that the attack of fever always followed excitement or tension. Contemplation of an impending examination in school was probably the most frequent offender, although the attacks had occurred after the excitement of attending a football game, or precedent to a trip or before coming home after a period away from it. Intercurrent infections, such as measles and chickenpox, were associated with excessive rises in temperature, and the boy was critically ill with each infection.

An incidental observation was that the eyes never teared during crying. He suffered from enuresis up to the age of 4 years. He was always considered to have a degree of muscular incoordination. He was unable to swim; he could not run, though he played at basketball, and he was rather adept at the piano. In his final summer it was observed that he staggered for several minutes after alighting from a subway train or on coming out of darkness into the light or out of light into darkness. The latter situation was particularly disabling. It appeared as though he could not adjust readily to any rapid change and this was one of them. Loud noises frightened him, and he was always considered to suffer from "vasomotor instability." When he perspired, it was noted that the left side of the forehead, and not the right, was covered with beads of perspiration.

Throughout his life the boy suffered from attacks of bronchial asthma. He had cutaneous tests for all the common foods at the age of 7 and was found to react positively to almost all of them. However, his diet was not restricted, and no clear association between food and the asthmatic attacks was ever demonstrated.

He had all sorts of medication for his various symptoms—among others, glandular therapy. Administration of chorionic gonadotropin at the age of 12 was associated with descent of the left testicle after the third injection.

An incidental observation was his pronounced fondness for hot foods, particularly for soups—foods that would upset him. His parents would request him not to take hot foods. During their eating he would perspire obviously on the left side of the forehead, and after ingestion he would become pale and dizzy and occasionally have to lie down for a short time.

As an infant he presented a difficult feeding problem, but at the age of 1 year he weighed 15 pounds (6.8 Kg.). Despite a voracious appetite he never seemed to gain weight normally. Eleven months before death, when nearly 17 years old, he was 4 feet 11 inches (149.9 cm.) tall and weighed 76 pounds (34.5 Kg.). He was generally underdeveloped, showing a small skeleton and poorly developed muscles. The penis and testicles were small, and the changes of puberty had not appeared. The underdevelopment was symmetric. Bone age was normal. His appearance essentially was that of a symmetric dwarf, since the underdevelopment seemed to involve the skeleton as well as the muscles.

The abnormal neurologic signs at the age of 17 years were as follows: The retinal arteries were tortuous. The eyes did not converge. There was weakness about the mouth; when he was asked to show the teeth, the upper lip was drawn laterally, the lower lip moving little, if at all. Speech was of the bulbar type, guttural in sound, as though the mouth were full. There was some drooling of saliva. He could not whistle. He was left handed, while the members of his family were right handed. Muscular development was retarded, and all movements lacked vigor. Breathing was largely diaphragmatic, since the intercostal muscles did not appear to move. There were lordosis of the lumbar portion of the spine and scoliosis of the dorsal portion. Resistance to passive movements was generally reduced. The range of passive movement of the joints was limited, and one could not flex or extend them completely. He could not raise the hands above the head. He walked stiffly, with the legs apart, weaving rarely to either side, the trunk bowed forward somewhat. It was impossible to obtain any of the deep reflexes.

He attended high school and took part in modified physical activities. He was bedfast only during the feverish episodes, the last of which had its onset ten days before death. He had taken his midsemester examinations. There then began the usual rhinitis, and on the eighth day the usual vomiting and abdominal cramping. The vomiting became retching, and the temperature ascended sharply to 103 F. As always during these attacks, he appeared desperately ill. Pentobarbital sodium, which had ameliorated some of the previous feverish attacks, failed to be effective. His temperature rose to 107 F. About twelve hours before death he was given morphine sulfate, ⅛ grain (8 mg.), after which he could never be aroused. This was thought to be the first dose of morphine that he had ever had. He ceased to excrete urine. Rales appeared in the chest, and he died.

Laboratory Data.—Psychologic examinations revealed intelligence quotients of 99 at the age of 5 years, 92 at the age of 6 years and 88 at the age of 13 years. Blood counts were normal. Reactions of the blood to the Wassermann and Kahn tests were negative. At the age of 6 years the sugar and the nonprotein nitrogen content of the blood were normal. Numerous roentgenographic studies of the chest and the gastroenteric tract showed nothing abnormal.

The blood pressure varied tremendously. Determinations during a day at the age of 9 years were as follows: Before breakfast, 88 systolic and 40 diastolic; at 3 p. m., in his father's office, 180 systolic and 130 diastolic; at

6 p. m., at home, 128 systolic and 60 diastolic; at 7 p. m., at home, 150 systolic and 100 diastolic, and at 8:30 a. m. on the following day, 150 systolic and 114 diastolic. The variability was as great throughout life; on one occasion, at the age of 16, it was 185 systolic and 150 diastolic; two months later, 128 systolic and 80 diastolic, and on the same afternoon, at a ball game, 152 systolic and 100 diastolic. The highest measurement was 220 systolic and 160 diastolic, less than one year before death. A day later the blood pressure was 120 systolic and 80 diastolic.

Clinical Diagnosis.—The clinical diagnosis was hypothalamic attacks of undetermined origin and amyotonia congenita.

Anatomic Diagnosis.—The anatomic changes, which will be described in detail in the accompanying article, were acute necrosis of the liver, minimal glomerulonephritis, asthmatic bronchitis and minimal acute bronchopneumonia, and "status thymicolymphaticus." In the nervous system, there was found an old lesion which had destroyed portions of the dorsomedial nucleus, the internal medullary lamina and the lateral nucleus of the right thalamus. Acute congestive changes and some perivascular hemorrhage were scattered throughout the central nervous system. The spinal cord showed changes in the anterior and lateral horns and in the posterior columns.

This boy had a nonprogressive, episodic disease, with onset in infancy. The nature of the attacks was discrete, and apparently each episode resembled the preceding one. It is stated that febrile attacks were provoked by emotional excitement. Each attack began abruptly, followed by elevation of temperature for several days, with pronounced fluctuations in temperature during this period, and, finally, by defervescence over the course of two or three days. With the onset of these attacks the patient would complain of coldness; he would shiver, and sometimes he had a chill. There was associated pallor of the face and extremities. The hands and feet were cold, the trunk warm. Sweating was absent. Piloerection was not noted. The sudden defervescence was marked by sudden, profuse sweating, warm extremities and flushing. The attacks were also associated with vomiting, nausea, diarrhea and pain in the extremities. There were formed elements, casts and albumin in the urine during the attacks, and the blood urea nitrogen level generally rose. The blood pressure fluctuated between hypertension and hypotension, but there was no consistent trend during the attack. Attacks were said to be aborted by pentobarbital, but it was also reported that the fever was reduced with antipyretic drugs. It was learned that this child had had a high temperature during attacks of measles and chickenpox. In all of the febrile attacks he was described as being extremely ill; during the period of rise in temperature he sometimes looked almost moribund.

Since the attacks of fever are important in the case, one might digress a bit to discuss heat regulation. The body temperature depends on a balance between heat dissipation and heat conservation and formation, and in the final analysis is controlled at the periphery.

Heat dissipation is mediated through the mechanisms of radiation, convection and conduction, and of evaporation of water from the surface. A body will radiate heat to neighboring structures which are at a lower temperature. Physiologically, this radiation is controlled by vasodilatation. By increasing the blood flow to the skin, a greater volume of circulating blood is brought nearer the surface, and hence there is a greater dissipation of heat. Evaporation of water from the surface leads to cooling. This is mediated chiefly through the mechanisms of sweating. A small amount of evaporation from the skin takes place without sweating, the so-called insensible water loss. In animals panting is important. These are the specific mechanisms of lowering body temperature.

Heat conservation is effected through (1) piloerection, which is not an effective means of heat conservation in human beings, and (2) peripheral vasoconstriction. In addition, the body can raise its temperature by increased heat formation; the most common mechanism by which this is done is increased muscular activity or shivering; shivering may become so marked as to constitute a chill. In addition, there may be an increase in general cellular metabolism. The latter plays an important role in the fever of infections, reaction to foreign proteins, etc.

Each of these factors may be modified by a number of things. When environmental temperature exceeds body temperature, radiation, convection and conduction can no longer be effective, and evaporation, through sweating, plays the major role. Peripheral changes which involve circulation and sweating will affect body temperature. Any morbid process or drug which causes prolonged peripheral vasoconstriction may cause the internal body temperature to rise. This was illustrated in a patient with a pheochromocytoma of the adrenal.[3] Similarly, drugs that cause increased sweating or increased peripheral circulation may lead to lowering of body temperature. It is not uncommon to see in dying patients a terminal rise in body temperature to 104 or 105 F., accompanied generally with marked pallor, vasoconstriction and

3. Engel, F. L.; Mencher, W. H., and Engel, G. L.: Epinephrine Shock as a Manifestation of Pheochromocytoma of the Adrenal Medulla, Am. J. M. Sc. **204**: 649-661, 1942.

cold hands and feet; actually, such persons are in shock. But their ability to dissipate heat is impaired because of the intense vasoconstriction, and in spite of the cold skin the rectal temperature may be high.

In studies of the central regulation of temperature, it has been well established that heat-regulating centers are located in the hypothalamus. In the anterior portion are located nuclei that have to do with heat dissipation. Stimulation of this area by galvanic current or by warming results in sweating and vasodilatation (and panting in animals). The destruction of this region in acute experiments results in hyperthemia, due to relative overactivity of the centers for heat conservation and formation, and in chronic preparations, in inability to adjust to high environmental temperature.

The centers for heat conservation and formation are located in the posterior portion of the hypothalamus, stimulation of which produces piloerection, shivering and vasoconstriction, destruction resulting in hypothermia and inability to adjust to lowered environmental temperatures. When both these hypothalamic centers are destroyed, varying degrees of poikilothermia may result.

From the clinical data on this patient, it is apparent that all means of temperature regulation were intact, but there seemed to have been some imbalance between the two functions. One is immediately struck with the similarity between the febrile attacks described here and those resulting from stimulation of the posterior hypothalamus or destruction of the anterior hypothalamus. In addition, the fact that these attacks were prevented by administration of pentobarbital focuses attention on the hypothalamus. Ranson and Clark [4] demonstrated that pentobarbital will inhibit the centers for heat formation and conservation in the posterior hypothalamus.

However, it is also known that this boy had flushing and sweating. This suggests that at first the posterior hypothalamus was stimulated, with resultant shivering, vasoconstriction and hyperthermia, and that then the anterior hypothalamus was stimulated and there resulted sweating, flushing and a fall in temperature. This alternation seemed to go on over a period of days, with rapid swings in temperature, until normal temperature was again restored. There must therefore have been some disturbance in the relationship between the two portions of the hypothalamus concerned with heat regulation.

At this point the question might be raised whether this boy had any other signs that might be ascribed to hypothalamic disturbance. Gastrointestinal symptoms such as those described as exhibited by this patient during his attacks have been demonstrated in animals on stimulation of the anterior hypothalamus.[1] The fluctuating hypertension suggests involvement of the blood pressure regulating mechanism in the posterior hypothalamus. Less certain to be of hypothalamic origin are the attacks of breath holding followed by somnolence, which in certain respects resembled narcolepsy or cataplexy. Hyperphagia has been produced in animals by hypothalamic lesions, but these animals usually become very obese.[5] This patient was almost a dwarf; we are not aware of the combination of hyperphagia and dwarfism being produced by hypothalamic lesions. Thus there are a number of symptoms which may definitely be related to the hypothalamus and others which might be.

To summarize the case thus far, we are dealing with a case of a nonprogressive, episodic disease in which our data suggest a disturbance in hypothalamic function and which was associated with a lesion in the thalamus on one side. Also, there was a generalized disturbance in the muscles, which were small and somewhat weak. The deep reflexes were lost, and there were lordosis, scoliosis, bulbar speech without evidence of bulbar palsy, drooling and defective convergence. Essentially, too, the boy was a symmetric dwarf. Smallness was not confined to the muscles, because the skeleton was also small. Osseous development, as measured by bone age, however, was normal.

Further, the boy had absence of secondary sex characteristics, no pubic hair and underdevelopment of the external genitalia. All these secondary abnormalities might be explained partially by the extreme loss in weight resulting from the repeated episodes of fever. He was said to have lost from 8 to 10 pounds with each attack. With such a handicap, it is obvious that this boy had to gain more than 100 pounds (45.4 Kg.) just to make up his periodic loss of weight, a fact which may also account for the muscular dystrophy. In short, these manifestations may have been indirect results of the central disturbance. Whether there was a more direct relation to the thalamic lesion and the hypothalamic dysfunction cannot be established from the data available.

It is clear from this analysis that in this case there was a paroxysmal disturbance in the central

4. Ranson, S. W., and Clark, G.: Neurogenic Fever Reduced by Nembutal, Proc. Soc. Exper. Biol. & Med. **39**:453-455, 1938.

5. Brobeck, J. R.; Tepperman, J., and Long, C. N. H.: Experimental Hypothalamic Hyperphagia in Albino Rat, Yale J. Biol. & Med. **15**:831-853, 1943.

regulation of body temperature, the circulatory system, the gastroenteric tract, respiration and sleep together with a more sustained derangement in somatic and secondary sexual development, which may have been at least partially secondary to the paroxysmal disturbance. This syndrome, which eventually proved fatal, was associated with a minute, fixed lesion of the right thalamus, which undoubtedly interrupted to some degree the connections of the hypothalamus with higher centers, and perhaps with lower vegetative centers.

The similarity between the symptoms experienced by this patient and the manifestations provoked in animals by stimulation of various portions of the hypothalamus admits of no argument; yet the hypothalamus in this patient was uninvolved. Indeed, had the hypothalamus been involved, one might anticipate a quite different clinical picture, characterized by a more or less fixed disturbance in vegetative function, and, in all likelihood, the boy would not have survived long after such damage had been sustained. It is of more than theoretic interest to inquire into the possible mechanisms of the attacks.

Penfield [2] referred to the attacks of hypothalamic activity experienced by a patient with an encapsulated tumor in the third ventricle pressing on the thalamus as "diencephalic autonomic epilepsy." In his patient, the attacks, which in certain respects resembled those experienced by our patient but were of much briefer duration and of more explosive character, could be adequately explained by variations in the degree of pressure by the tumor on the thalamus. In this sense the tumor could be regarded as a local source of irritation which provoked a discharge, either by involvement of a higher neural pathway or by direct involvement of the hypothalamus. The concept implicit in the term "epilepsy" appears valid in such an instance.

In our case no such mechanical factor can be invoked. One might consider the lesion analogous to a cortical cicatrix secondary to craniocerebral injury, and as such an epileptogenic focus. The hypothalamus, however, is not analogous to the cortex. As the main center for the mediation of autonomic function, it is under the constant influence of both excitatory and inhibitory impulses from higher centers and of afferent impulses from the periphery. The lesion in the thalamus acted to interrupt to some degree the higher cortical control of hypothalamic function. This could lead to overreaction of this region to the continuous inflow of afferent impulses, a release phenomenon in the sense defined by Hughlings Jackson. Analysis of the provocative factors of the various attacks tends to confirm this interpretation. Stimuli that normally lead to febrile responses, such as intercurrent infections, in this boy led to excessive rises in temperature. Some emotional experiences which ordinarily are expressed through various changes of a vegetative nature, provoked caricatures of such reactions. The attacks were not "spontaneous," but were all tripped off, sometimes by situations obviously charged with anxiety, sometimes by more subtle provocation. The dynamics involved in this case can thus be fully clarified only by a more detailed analysis of some of the psychodynamic factors.

PSYCHIATRIC DATA

No detailed psychiatric evaluation in this case was made during life. The following rather fragmentary observations were reconstructed in retrospect.

The patient was born four to five weeks prematurely, the younger of 2 sons of a pediatrician. The first born was 4 years older than the patient and was normal in all respects except for a labile blood pressure, from which the mother also suffered. The father was energetic and ambitious and stuttered somewhat. From birth the child was considered abnormal; early he presented a difficult feeding problem. Later the underdevelopment and dwarfism, the asthma, the difficulty in muscular coordination and the bizarre attacks all served to set him apart from his older brother and from other children. The anxiety of the parents was understandable and was indicated by the weight of medical attention with which the child had to cope, practically since birth—only a little of it is detailed in the medical history.

Despite these intellectual, physical and psychologic handicaps, the boy tried to compete with normal children. He trained in regular school, was taken into a boy scout troop, played in piano recitals and took part in other competitions. There is every indication that he felt a strong need to demonstrate his ability and to deny his disabilities. It is usual to find that the prolongedly ill child either remains infantile or acquires an attitude of complete denial of the illness. The latter, rather, was the case with this boy; yet, at the same time, he was repetitively faced with new and confusing medical examinations, which served greatly to entrench his feelings of insecurity and to expose to him the family's underlying anxiety. As has any child with a chronic disability, he had a greater need for love and reassurance. Actually, he repeatedly participated in group activities, where he had difficulty in holding his own. Frustration and conflict are easily understandable in such circumstances. Rage and resentment were not expressed verbally. The child was extremely obedient and amenable to any suggestion or request. It is noteworthy that the episodes of breath holding usually occurred in circumstances in which anger was likely.

Comments by two of the psychologists who were asked to estimate the intellectual attainment of this boy are of some interest. When the patient was 5 years old, one noted: "The examiner is inclined to believe that

the boy could do better if he had more confidence in himself. A pitiful, faint whisper, 'I don't know,' was generally his first reply. . . . He will certainly profit more by being taught at home, and where he is allowed to express his own ideas, than he will in a large group of children. He needs constant encouragement, but also the companionship of other children." When the patient was 13, another examiner noted: "An interesting sidelight occurred in the free association test for the age of 10 years. The word 'school' was followed by 'unhappy,' and later the word 'happy' brought forth 'baseball,' 'field' and 'game.'" These comments reveal the child's deep-seated insecurity, as well as some of the conflicts he experienced with respect to school and play. While these responses would not be uncommon among normal children of this age group, in this child they tend to confirm the impression of rebellion against the level at which he was expected to compete, a level which served as a denial of his disability.

Some of the situations which appeared to precipitate attacks are of interest. Contemplation of an impending examination in school was probably the most frequent offender, although the episodes also occurred after the excitement of attending a football game, preceding a trip or before coming home after a period away from it. These are circumstances that might be expected to provoke excitement, and even anxiety, in normal children. That they had an even greater impact on this boy and that his defenses were less adequate is highly probable.

In retrospect, it would be hard to imagine how his psychologic development could have been more battered by the medical handling he received. He was treated in a manner which would mobilize anxiety, but he had little means of handling it. His immediate environment demanded that he display none of it. In addition, he had a deficit in certain nervous structures which further impaired his ability to allay anxiety. At no time during his long contact with medical aid did the problem of his emotional adjustment to his disability appear to receive much thought.

The relation of the feverish attacks to what were for this boy strenuous and intolerable situations was repeatedly demonstrated to the satisfaction of those who had the most to do with him. Psychogenic factors certainly initiated many of the attacks, the final of which resulted in death.

The patient had a lesion of the right thalamus which apparently partially interrupted corticohypothalamic connections. It is well established that the hypothalamus is the main way station for the autonomic reactions that accompany the expression of emotions. These autonomic reactions normally serve the useful purposes of preparing the organism for the activities required for fighting, fleeing, acquisition of food, mating, and the like, and, as goal-directed activities, are under higher cortical control.[1a] In this patient, it may be postulated that this higher cortical control was incomplete because of the interruption of neural pathways.

The patient was subjected to considerable environmental stress of an anxiety-provoking character. This sick lad produced a blow to his family's self esteem, to which the latter never adjusted. The patient's early anxieties were the result of family anxieties and were of such magnitude that one would expect a structurally normal child in comparable circumstances also to manifest neurotic reactions. Unquestionably, the child felt rejected since he could not come up to family standards. Because of family attitudes, he felt an overwhelming need to act and behave as a normal child. The ordinary dependent and infantile longings of any child for security were repressed in him.

The boy found himself in one situation after another which provoked anxiety in him (school, scouting, competitions), but, because of the interruption of the corticohypothalamic pathways, the autonomic manifestations of the anxiety went far beyond normal expression, both qualitatively and quantitatively, and resulted in the clinical picture and finally in death. Why distortions of some hypothalamic activities (notably temperature regulation) were more prominent than others is not clear, but the marked tendency to overshoot in either direction is consistent with the absence of normal moderating influences. In other words, because of the structural lesion, the response was poorly directed, excessive and uneconomical, tended to be self perpetuating and was essentially destructive, rather than protective, to the patient. This was true whether the reaction was initiated by psychologic factors (anxiety), physiologic factors (intercurrent infection) or a combination of the two.

Clearly, proper therapy should have been directed toward protecting the patient from anxiety-producing situations until he might have developed better defenses to handle his disability. Denial was not an effective means of doing this. It is worth pointing out that experimental animals with chronic hypothalamic lesions may get along well if not put under environmental stress.

Obviously, this explosive type of autonomic reaction in response to psychogenic or physiogenic stimuli is not confined to patients with lesions of the central nervous system involving hypothalamic connections. A comparable example of an explosive sympathetic discharge provoked by similar factors may be cited[3] in a patient with an epinephrine-secreting tumor of the adrenal medulla (pheochromocytoma). Indeed, comparable mechanisms for the production of "attacks" in many diseases (e. g., epilepsy, migraine, cardiac disorders) in the presence of a great variety of structural lesions involving many different organ systems could be cited.

This case demonstrates the importance of a liberal and dynamic approach to the interpretation of symptoms. The demonstration of the lesion in the thalamus provided a starting point, but nothing more, for an understanding of symptom formation in this patient.

SUMMARY

An 18 year old boy had recurrent attacks of coryza, chills, fever, nausea, vomiting, abdominal cramps, oliguria, fluctuating hypertension, tachycardia and muscle cramps, beginning at the age of 5 months. The patient eventually died during such an attack. The attacks developed during anxiety-provoking situations or in the course of intercurrent infections. The patient also had frequent episodes of breath holding, cyanosis and unconsciousness, followed by somnolence, which began on the third day of life. He also had bronchial asthma and pronounced skeletal, muscular and genital underdevelopment.

Postmortem examination revealed a small cystic softening involving portions of the dorsomedial nucleus, the internal medullary lamina and the lateral nucleus of the right thalamus. The hypothalamus was intact.

The lesion interrupted partially corticohypothalamic connections and led to distortion and exaggeration of hypothalamic reaction in response to physiogenic and psychogenic stimuli. An analysis of psychodynamic factors revealed the importance of anxiety in provoking poorly moderated and directed hypothalamic responses.

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HYPOTHALAMIC ATTACKS WITH THALAMIC LESION

II. ANATOMIC CONSIDERATIONS

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An extensive neuropathologic study was undertaken on a young man aged 17¾, who died in one of an extended series of attacks of hyperthermia. He had been studied rather exhaustively clinically, having been examined by more than one hundred physicians; it was recognized during the latter part of his life that the attacks from which he suffered were most likely due to disturbed hypothalamic function.

Since the study appeared to cast some light on thalamic and hypothalamic function, and more on hypothalamic regulation, it was deemed advisable to record the neurohistologic findings in some detail. The clinical data and the physiologic and psychosomatic aspects were discussed in the foregoing article.[1]

PATHOLOGIC REPORT

Postmortem Examination.—The examination was performed two hours after death. The body was that of a small, somewhat poorly nourished white male whose size and conformation suggested an age not over 12 or 14 years. The hair was sparse except on the head and was normally distributed.

The genitalia were immature; the testes and epididymides were distinctly smaller than normal. The prostate gland was infantile in size and was compressed and scarcely recognizable. The adrenal glands were somewhat smaller than average. The thymus was distinctly large, measuring 10 cm. in length and varying in width from 1 to 3 cm. and in thickness from 0.5 to 1.5 cm. The spleen was moderately enlarged.

All extremities were of proportionate size and development. There were some clubbing of the finger tips and reddening of the distal phalanges. The muscular tissue everywhere appeared grossly diminished in amount; there was no focal muscular atrophy.

Microscopic Examination of the Viscera.—Exclusive of changes in the nervous system, the micropathologic findings consisted of a moderate degree of focal acute pneumonitis, chiefly peribronchial in distribution. There was marked thickening of the bronchial walls due to proliferation of connective tissue and infiltration with lymphocytes and eosinophils. The basement membrane was thick and hyalinized, beneath an intact bronchial mucosa. The latter changes were considered to be consistent with those of an allergic form of bronchitis.

In the liver numerous scattered areas of focal necrosis were found, chiefly in the central zones, and they were associated with infiltration of polymorphonuclear leukocytes. The tissue necrosis was an acute reaction, without evidence of scarring or repair. In the severe lesions only phantoms of liver cells remained. The liver tissue which remained intact presented acute passive congestion. There was no abscess formation or retention of bile.

There was moderate congestion of the kidneys. Occasional small areas of scarring involved the tubular and interstitial tissue, and an occasional glomerulus was reduced to a fibrous ball. Sometimes concentric scarring was seen around Bowman's capsule.

The adrenal glands were microscopically normal except for vascular engorgement.

Some hyperplastic reticulum was seen toward the central portion of the thymic lobules. Structures suggestive of Hassall corpuscles, with degenerative changes, were noted. There was pronounced congestion of the thymus gland.

Sections of hilar, aortic and mesenteric lymph nodes contained greatly dilated sinusoids and hyperplastic reticulum and endothelium. Remnants of follicles were seen; there were old and recent degenerative changes. There were scattered chromatin flecks, necrosis of cells and, in places, cellular infiltration. The older change was indicated by hyalinization and scarring. Congestion was marked throughout.

In the spleen the majority of malpighian bodies showed central degenerative changes, principally hyalinization and scarring. Superimposed on the chronic change were acute alterations, consisting of chromatin flecking and vascular engorgement.

Sections from the gastrocnemius muscle revealed no abnormality. The pituitary gland was normal.

Macroscopic Examination of the Central Nervous System.—All the surfaces of the brain were congested. The development of the cortex appeared normal. The blood vessels of the circle of Willis were of normal distribution and did not show structural change.

Vertical sections of the brain were made at 6 mm. intervals. Congestion of all vessels was noted. A small cystic cavity within the dorsomedial and lateral nuclei of the right thalamus was found (fig. 1), which measured 9 by 1.5 by 2 mm. The long axis of the cavity was on the oblique plane of a projected line drawn from the inferior aspect of the third frontal convolution (dorsally) to the ventralmost aspect of the third ventricle (ventrally), where it extended to within 3 mm. of the ependymal lining of the third ventricle (fig. 1). Dorsally it reached to within 5 mm. of the border between

From the Departments of Internal Medicine (Neurology) and Psychiatry, University of Cincinnati College of Medicine, and the Laboratory of Neuropathology, Cincinnati General Hospital.

1. Engel, G. L., and Aring, C. D.: Hypothalamic Attacks with Thalamic Lesion: I. Physiologic and Psychologic Considerations, Arch. Neurol. & Psychiat., this issue, p. 37.

the external capsule and the lateral aspect of the lateral thalamic nucleus. The nerve tissue immediately adjacent to the cavity appeared homogeneous and was slightly firm to touch.

The remaining portions of the central nervous system showed no gross abnormalities.

Microscopic Examination of the Central Nervous System.—Sections from many cortical areas, from the thalamus on both sides, from the hypothalamic region, from the cerebellum, from six levels of the pons and medulla and from eight levels of the spinal cord (first, fourth and eighth cervical; second, fourth and eighth dorsal, and first and fifth lumbar) were stained with hematoxylin and eosin, cresyl violet and the Loyez, Bodian 1 per cent strong protein silver and silver carbonate methods. From the pituitary gland, sections including the anterior and posterior lobes and the intermediate area were stained by the Biggart technic.

were slightly but definitely larger than those on the right (fig. 1). On the right the lateral portion of the dorsomedial nucleus and a small bit of the mesial portion of the lateral nucleus of the thalamus were destroyed by a cyst which has already been described. The cyst cavity extended across the midportion of the internal medullary lamina and roughly was estimated to destroy about 5 per cent of the lateral nucleus and about 50 per cent of the dorsomedial nucleus of the right thalamus. In serial sections of the thalamic nuclei the cyst occupied a more dorsomedial portion the more posteriorly one examined, though it nowhere communicated with the third ventricle.

Demyelination of the fibers of the right dorsomedial nucleus was massive and extended to the periependymal fibers running from this nucleus to the hypothalamus. Other periependymal fibers running to the stria medullaris and the habenular ganglion were involved. The

Fig. 1.—Vertical section through the dorsomedial nuclei of the thalamus. Note the cyst which has destroyed the cellularity of the ventral half of the right dorsomedial nucleus and which traverses the internal medullary lamina to involve slightly the lateral nucleus. Congestion is also shown. Loyez stain; × 5.

There were marked congestion of all vessels throughout the central nervous system and scattered areas of diapedesis, more numerous in the brain stem. On one side of the medulla, at the midolivary level, clusters of punctate hemorrhages were located in the dorsal motor nucleus of the vagus nerve. In sections stained with cresyl violet it was possible to determine that these hemorrhages had existed long enough to cause destruction of about one-half the cells of this strategic nucleus; some of the remaining cells were shrunken in appearance. There had also been a perivascular extravasation of similar type in the descending autonomic bundle (the dorsal longitudinal fasciculus of Schütz). The cerebrum and cerebellum were normal except for the acute changes associated with severe congestion.

The left thalamus showed no abnormality except for vascular engorgement. The thalamic nuclei on the left

fibers from the right medial nucleus of the thalamus to the association areas of the frontal lobe, i. e., those comprising the right anterior thalamic radiation, were demyelinated. The medullary striae, the centrum medianum and the subthalamic structures were normal bilaterally.

The inner surface of the cystic cavity was sharply outlined by a thin membrane formed by glial nuclei and strands of glial fibers, loosely adherent to the inner wall of the cavity (fig. 2), which contained a few congested, small blood vessels. No gitter cells or signs of inflammation were present.

The tissue immediately surrounding the cyst showed marked disorganization, where the large majority of nerve cells were destroyed. Those remaining showed far advanced degeneration; they had undergone almost complete calcification (fig. 2).

The affected nerve cells could be identified only by their shape and size. They stained a deep, rather uniform black in silver preparations, which delineated them as irregularly nodular (figs. 2 and 3). The nodularity extended throughout the body and processes of the cells to such distances as the processes had taken the stain. It appeared as though neurofibrillary material had swollen, fragmented and filled the cell. The neuronal change, clearly defined in the silver stains only, became less obvious as one examined progressively away from the cyst, and could be barely identified in the cell stains, where the cells appeared shadowy and vacuolated.

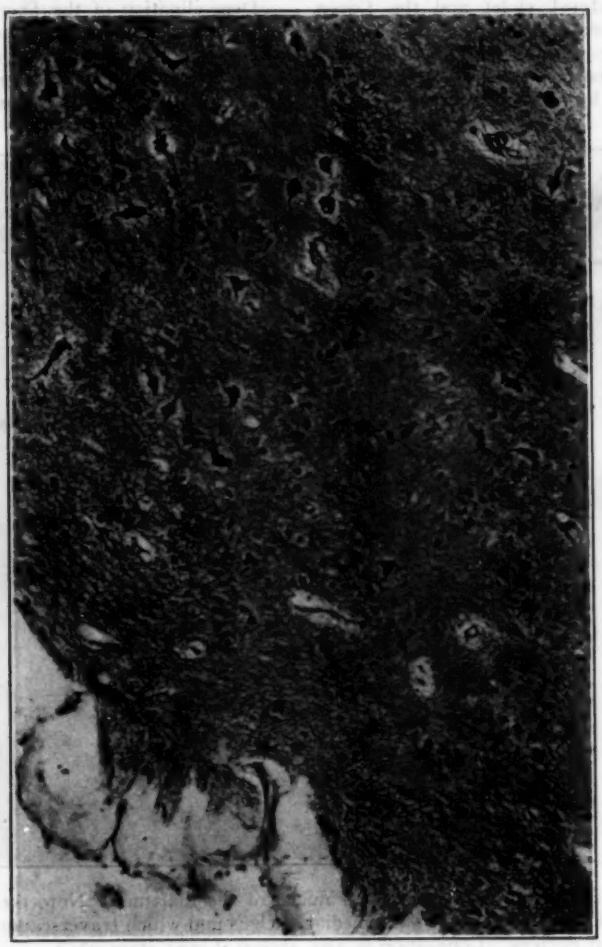

Fig. 2.—A portion of the right dorsomedial nucleus of the thalamus, bordering on the cyst. Note the loosely adherent membrane lining the cavity of the cyst and the loss of nerve cells and fibers. The nerve cells remaining are calcified. Bodian stain; × 160.

Nuclei or nucleoli could not be discerned in any of the involved cells.

In addition to calcified thalamic nerve cells, the abnormal tissue was composed of large masses of irregularly arranged glial cells. There were some mature astrocytes recognizable. The wall of the third ventricle immediately adjacent to the cyst was lined by ependymal cells, beneath which several layers of bipolar spongioblasts were arranged parallel to the ventricular wall. No nerve cells or myelinated fibers could be found in the paraventricular region mesial to the cyst. Axis-cylinder preparations of this area revealed the almost complete absence of nerve fibers. The dorsal half of the dorsomedial thalamic nucleus showed no change, and the other thalamic nuclei, except the mesial bit of the lateral nucleus, appeared normal.

All of the hypothalamic nuclei were examined carefully and were normal. The structures of the mesencephalon, the inferior and superior colliculi and the tegmentum were normal. The brachium conjunctivum contained a normal complement of fibers. The red nuclei as well as the nuclei of the cranial nerves were normally developed, and the nerve cells were well preserved except for the acute change noted in the vagus nucleus on one side. The aqueduct of Sylvius and the adjacent gray substance disclosed no pathologic change.

All of the cerebellar peduncles were normal. Within the lateral portion of the reticular formation on one side of the pons and medulla, there was a slight but definite decrease in nerve fibers and myelin sheaths, as compared with the same structures on the opposite side. This destruction was probably of a descending bundle of fibers which stream out of the posterior hypothalamus and which are probably primarily orthosympathetic. They take up a fairly diffuse position in the reticular formation.

In the cervical and upper thoracic segments of the spinal cord there has occurred almost complete destruction of the nerve cells of the lateral horn on one side. The few remaining cells disclosed marked degenerative

changes with neuronophagia. The sympathetic cells of the opposite side were in a moderately good state of preservation.

Myelin sheath preparations revealed that in the first cervical segment of the spinal cord, in the concavity between the dorsal horn and the lateral projection of gray substance (lateral fasciculus proprius) on one side, there was a circumscribed area of demyelination (fig. 4) implicating a small number of longitudinally running fibers which were intimately interlaced with the gray substance. Some of these myelin sheaths were broken into globules. The nerve cells in the lateral gray substance were destroyed on the same side.

segments of the spinal cord. In some areas there was complete lack of large anterior horn cells. The remaining cells disclosed satellitosis and neuronophagia. There was a slight increase of small glial cells. All changes were more pronounced in the anterior horns on the same side as the damage to the lateral horn.

In the lower thoracic, lumbar and sacral segments the nerve cells were in a moderately good state of preservation, though possibly slightly reduced in number.

There was moderate loss of myelin in the posterior columns of the spinal cord throughout its length, more marked in the fasciculus cuneatus than in the fasciculus gracilis. The loss of myelin sheaths was most obvious

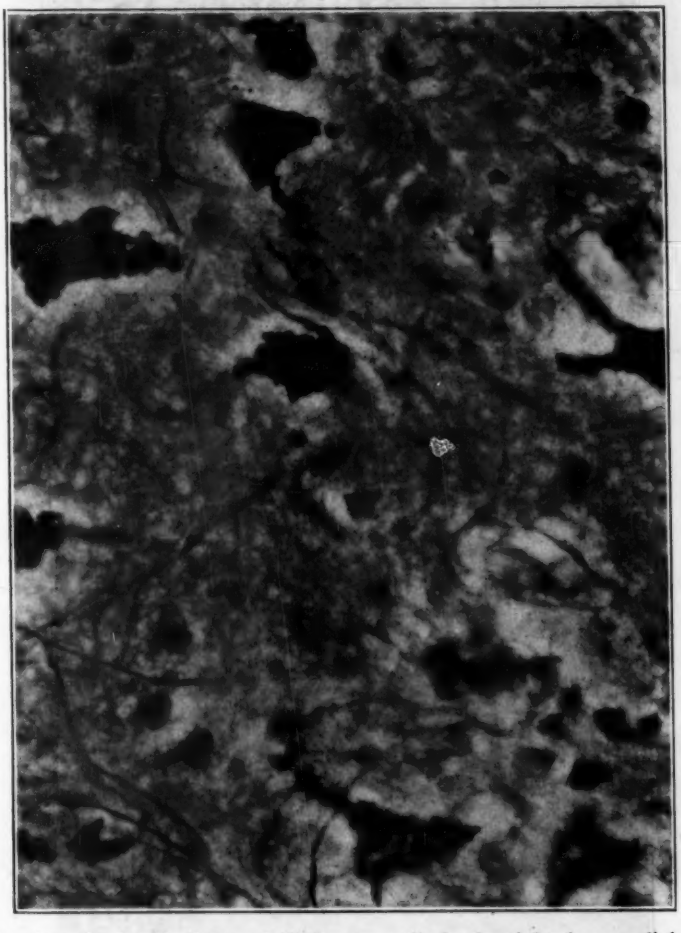

Fig. 3.—Section showing the detail of the calcified nerve cells in the right dorsomedial nucleus of the thalamus and the paucity of nerve fibers. Bodian stain; × 1,000.

This region, which appeared pale in myelin sheath preparations, showed a reduction of nerve fibers (fig. 5) in the sections impregnated with silver according to the Bodian method. Some of the remaining axons were either irregularly swollen or considerably reduced in size.[2] Comparable areas in the gray and white matter on the opposite side of the cervical segments of the spinal cord were normal. The anterior horn cells were reduced in number throughout the cervical and upper dorsal

2. Dr. A. M. Lassek, professor of anatomy, Medical College of the State of South Carolina, when shown these sections, noted the destruction of cells of the lateral substance and nearby tracts on one side. He noted the close relation of the fibers in question to the pyramidal tract and said there was no known tract in this vicinity.

immediately adjacent to the gray matter of the posterior horns and the gray commissure. The spinal roots were normal until they entered the spinal cord, at which point it seemed that some degeneration had occurred.

In summary of the pathologic changes in the nervous system, there was found an old lesion which destroyed the ventral half of the dorsomedial nucleus and a bit of the internal medullary lamina and of the lateral nucleus of the thalamus on the right. There was rarefaction in the reticular substance of one side as it traversed the regions of the pons, medulla and upper cervical segments of the cord. The cells

in the lateral gray matter and the lateral horns on one side of the cervical and upper thoracic segments of the spinal cord were destroyed. The anterior horn cells of the spinal cord were affected, especially those of the rostral portion of the cord. There was some demyelination of the white matter of the posterior columns of the spinal cord. Acute congestive changes were seen throughout the central nervous system.

Fig. 4.—Discrete demyelination in the lateral fasciculus proprius of one side of the first cervical segment of the spinal cord. (To the left is gray matter; to the right, white matter). Loyez stain; × 160.

Findings outside the nervous system included acute necrosis of the liver, minimal glomerulonephritis, asthmatic bronchitis and minimal acute bronchopneumonia and the condition which has been termed by some "status thymolymphaticus."

COMMENT ON CLINICOANATOMIC FEATURES

The unilateral deterioration of long tracts in the reticular substance of the pons, medulla and upper cervical segments of the cord, associated with destruction of cells in the lateral gray matter and in the lateral horns of the cervical and upper thoracic segments of the spinal cord, deserves a word. The inference is that a system of fibers and cells was affected in a long-standing degenerative process and that the localities involved are those harboring structures subserving autonomic function.

Magoun [3] has described a pathway in the brain stem of cats which descends either directly or through relays to preganglionic sympathetic neurons in the spinal cord. This pathway arises from the lateral hypothalamic area, and in the medulla it is distributed chiefly in the lateral portion of the reticular formation; thence it

3. Magoun, H. W.: Descending Connections from the Hypothalamus, A. Research Nerv. & Ment. Dis., Proc. **20**:270-285, 1939.

descends in the anterolateral funiculus of the upper cervical portion of the cord. List and Peet [4] concluded that in man descending hypothalamic paths were located in analogous areas.

What the lesions of the brain stem and cord had to do in this case with the labile control of temperature and blood pressure and the periodically abnormal respiratory function, gastroenteric mobility, urinary output and content and unilateral sweating on the forehead cannot be stated. One might consider that imbalance in the innervation of structures concerned with these functions might have been brought about more readily in the presence of a disorder of the central nervous system such as this.

It is of extreme importance that a unilateral lesion in the thalamus may be associated with hypothalamic attacks. In this case, the hypothalamus was structurally normal; yet emotional factors, as well as infectious disease, provoked its functional disturbance. It seems clear that, through the interruption of certain higher pathways, it is possible to disturb hypothalamic function. In other words, the hypothalamus may be released, in the sense that Hughlings Jackson was the first to enunciate.

Fig. 5—Swelling and reduction of axons in the lateral fasciculus proprius of one side of the first cervical segment of the spinal cord, from a section contiguous to that shown in figure 4. Bodian stain; × 160.

If there were doubt that the hypothalamus was at fault during the attacks suffered by this boy, it should be noted that some hyperthermic episodes could be aborted with pentobarbital. As Ranson and Clark [5] have so clearly shown, a site of action of this barbiturate in man or animal may be the hypothalamus, with the resultant prevention of hyperthermia after surgical manipulations in this region.

4. List, C. F., and Peet, M. M.: Sweat Secretion in Man: V. Disturbances of Sweat Secretion with Lesions of the Pons, Medulla, and Cervical Portion of Cord, Arch. Neurol. & Psychiat. **42**:1098-1127 (Dec.) 1939.

5. Ranson, S. W., and Clark, G.: Neurogenic Fever Reduced by Nembutal, Proc. Soc. Exper. Biol. & Med. **39**:453-455, 1938.

What is known about relays between the cerebral cortex and the diencephalon? The association nuclei of the thalamus that have numerous connections with other diencephalic nuclei and project to association areas of the cerebral cortex (parietal and prefrontal) are the dorsomedial and lateral nuclei and the pulvinar. The functions of these associations possibly are inferable from their anatomic connections, and therefore the dorsomedial and lateral thalamic nuclei are thought to be concerned in some fashion in corticohypothalamic association.

At this point it may be worth recalling that pathologic studies [6] of brains that had undergone prefrontal lobotomy revealed trivial cortical damage, but the dorsomedial nucleus of the thalamus suffered severe retrograde changes, characterized by the loss of most of its cells. Further, these studies by Freeman and Watts indicate that the pathway interrupted by lobotomy is predominantly thalamofrontal, rather than frontothalamic.

An analysis of this case lends evidence that the dorsomedial thalamic nucleus transmits fibers which aid in the control of nervous function at lower levels. Possibly the clinical syndrome would not have been so readily provoked if something had not been the matter with nervous mechanisms in the brain stem and the spinal cord. The latter lesions may require consideration in any thinking about hypothalamic release by a lesion rostral to the hypothalamus, and unilateral only.

SUMMARY

The histopathologic study of a 17¾ year old boy who was for years subject to attacks of hypothalamic dysfunction revealed an old lesion which destroyed the ventral half of the right dorsomedial nucleus of the thalamus. It is thought that analysis of this case lends evidence that this thalamic nucleus transmits corticohypothalamic connections. In the face of a usually symptomless but fixed thalamic lesion, normal hypothalamic regulation was rather easily disturbed by emotional factors or by infections.

6. Freeman, W., and Watts, J. W.: Physiological Psychology, in Luck, J. M.: Annual Review of Physiology, Stanford University, Calif., Annual Reviews, Inc., 1944, vol. 6, pp. 517-542.

THYROID FUNCTION OF MANIC-DEPRESSIVE PATIENTS EVALUATED BY DETERMINATIONS OF THE SERUM IODINE

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Previous investigators have endeavored to discover any relation between manic or depressive states and function of the thyroid gland by determination of the basal metabolic rates of patients with such conditions.[1] It is impossible to obtain reliable and accurate basal metabolic rates for overactive or apprehensive patients. For patients without psychosis, the concentration of iodine in the serum has proved to be an extremely accurate criterion of thyroid activity. In a study of several hundred subjects with and without thyroid disease, values for serum iodine below 3 micrograms per hundred cubic centimeters indicated hypofunction,[2] and values above 9 micrograms per hundred cubic centimeters denoted overactivity of the thyroid gland. Conversely, serum iodine concentrations within the limits of 3 and 8 micrograms per hundred cubic centimeters were almost never observed for subjects with definite abnormality of thyroid function. Values between 8 and 9 micrograms per hundred cubic centimeters were obtained both for patients with hyperthyroidism and for normal subjects. There is good reason to believe that the precipitable iodine in the serum is closely related to, if not identical with, the concentration of iodine in the circulating thyroid hormone. In those patients to whom no inorganic iodine has been given, the precipitable iodine of the serum is usually between zero and 1 microgram per hundred cubic centimeters lower than the total iodine of the serum. Determination of the serum iodine has proved to be a more reliable test in the diagnosis of myxedema than the evaluation either of the basal metabolic rate or of the cholesterol concentration of the serum.[3] In cases of hyperthyroidism the serum cholesterol concentration is of little diagnostic aid[4]; the basal metabolic rate is of more value, but in doubtful cases the serum iodine concentration has proved the most reliable guide.[2]

In the present investigation, thyroid activity as measured by serum iodine determinations has been evaluated in 26 manic-depressive and in 17 depressed patients who were not typical manic-depressive persons. Nine of the manic-depressive patients were in a manic state. Eight of the non-manic-depressive patients were seen in agitated depressions.

SUBJECTS

The histories of all 43 patients were carefully reviewed, and only the patients who were clearly manic-depressive were included in the first group. These patients were considered manic-depressive because there occurred definite ups and downs (periodicity) in their life courses. In addition, at the time of unmistakable breakdowns they manifested the classic triads of manic-depressive disturbances, which are sadness and retardation of motor activity and thought, or euphoria with hyperactivity and flight of ideas. Our notion of the manic-depressive personality implies that the person is born and dies with such a manic-depressive trend even though he never has what is called a psychosis.

These subjects have been patients during the past five years. No attempt was made to determine the serum iodine concentration for every patient with a manic or a depressed condition. The patients whose serum iodine concentrations were determined were persons who were suspected of having an abnormality of the thyroid and who clinically showed one or more of the following symptoms: palpable thyroid; questionable exophthalmos, tachycardia or tremor; abnormal obesity; thick skin or puffy eyes; thin, coarse hair, and a facial expression suggestive of myxedema. Thus, of 250 to 300 patients with a manic-depressive or otherwise depressive disorder admitted during these five years, determinations of the serum iodine of only 43 are included in this study. It is scarcely necessary to say that in the whole group the

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1. Bowman, K. M., and Grabfield, G. P.: Basal Metabolism in Mental Disease, Arch. Neurol. & Psychiat. **9**:358 (March) 1923. Gibbs, C. E., and Lemcke, D.: Study in Basal Metabolism in Dementia Praecox and Manic-Depressive Psychoses, Arch. Int. Med. **31**:102 (Jan.) 1923. Farr, C. B.: Results of Basal Metabolism Tests in One Hundred Mental Cases, Arch. Neurol. & Psychiat. **12**:518 (Nov.) 1924; Basal Metabolism in the Psychoses, A. Research Nerv. & Ment. Dis., Proc. **11**: 221, 1931.

2. Winkler, A. W., and Man, E. B.: Serum Iodines in Subjects Without Definite Clinical Evidence of Thyroid Disease and in Those With Simple Goiter, to be published.

3. Riggs, D. S.; Man, E. B., and Winkler, A. W.: Serum Iodine in Myxedema Before and During Thyroid Medication, J. Clin. Investigation, to be published.

4. Man, E. B.: Gildea, E. F., and Peters, J. P.: Serum Lipoids and Proteins in Hyperthyroidism, J. Clin. Investigation **19**:43, 1940.

incidence of clinical signs suggesting thyroid dysfunction must have been relatively lower.

The ages of the subjects ranged from 21 to 63 years. Eight were men and 35 women. Three patients whose cases will be presented in detail (figs. 2, 3 and 4) were believed to have had true hyperthyroidism and had thyroidectomies during observation on our service. Of the remaining 40 patients, 8 had a palpable or somewhat enlarged thyroid; 6 had slight exophthalmos, and 7 had had a previous thyroidectomy.

Of the 3 patients who presented the clinical picture of hyperthyroidism, the first 2 (figs. 2 and 3) were manic-depressive patients in a hypomanic phase, and the third (fig. 4), who was not a typical manic-depressive patient, had a depression with agitation. The diagnosis of hyperthyroidism was confirmed by the pathologic reports on 2 of these subjects (cases 1 and 2). The third patient was given strong solution of iodine U. S. P. for two months prior to thyroidectomy. No hyperplasia was observed in the excised gland, which showed complete involution, with adenomatous masses, some of which had apparently degenerated. Considering the duration of iodine therapy, the pathologic observations did not refute, but could not confirm, the clinical diagnosis of hyperthyroidism.

Serum iodines, either total or precipitable, were determined by the Riggs and Man potassium permanganate acid ashing method,[5] with modifications published later.[6]

All iodine determinations were made on precipitated serums when patients were under iodine therapy. At other times, the serum iodine was determined as total iodine in some cases and as precipitable iodine in others. In these instances no differentiation has been made between total and precipitable iodines because the amount of inorganic iodine in serum is minute unless iodine therapy or contamination has occurred. Serum cholesterols were determined by a gravimetric digitonin procedure.[7] Blood was drawn without stasis from the antecubital vein when the patient was in the postabsorptive state before breakfast. Basal metabolic rates were determined with Collins' Benedict-Roth or Sanborn's motorgraphic modification of the Benedict apparatus.

RESULTS

In figure 1 the distribution of iodine values for the 43 patients is shown. Only one value is given for each patient. When more than one determination of serum iodine was made, an average value was used, except that only the initial values are presented for the 3 patients who had thyroidectomies on our service. With the omission of these 3, 36 of the 40 patients had serum iodine values within the normal range of 3 to 8 micrograms per hundred cubic centimeters. In view of the limited number of studies, the general incidence of the values for the 36 patients follows the trend of a normal distribution curve. The iodine values for 27 of the 36 patients fell within 4.5 and 6.5 micrograms per hundred cubic centimeters, the middle of the normal range.

Values for the serum iodine of 22 of the 26 manic-depressive patients fell within the normal range of 3 to 8 micrograms per hundred cubic centimeters. The iodine values for the other 4 subjects were all above 8 micrograms per hundred cubic centimeters. Two of the subjects had outspoken clinical hyperthyroidism and were treated by subtotal thyroidectomy. The serum iodine concentration for a third subject was 8.1 micrograms per hundred cubic centimeters, a borderline value which does not exceed the normal range by the experimental error of the method. The fourth patient, with a serum iodine level above 8 micrograms per hundred cubic centimeters, was a depressed, 49 year old man. About four months before his admission to the New Haven Hospital, he had been suspected of hyperthyroidism and had been given strong solution of iodine U.S.P. for a couple of months. At the time of his admission there were no clearcut symptoms of hyperthyroidism, but the serum iodine concentration was 12.2 micrograms per hundred cubic centimeters. From the history the suspicion is strong that he had true clinical hyperthyroidism with some remission of activity at the time the value for serum iodine was obtained. The number of patients is too small to permit comparison of concentrations of iodine in serum taken in a manic phase with the concentrations of iodine in serum taken in a de-

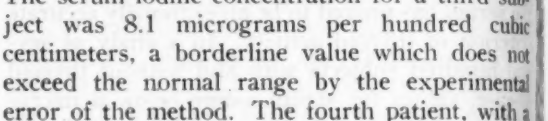

Fig. 1.—Serum iodine concentrations for 26 manic-depressive patients and 17 patients with depression. The barred squares represent values for 9 subjects in the manic phase; the double-hatched squares, values for 17 subjects in the depressed phase of the manic-depressive disturbance; the single-hatched squares, values for 8 subjects with agitated depressions that were not considered manic-depressive disturbances, and the open squares, values for 9 subjects with depressions who did not have a manic-depressive condition.

The 3 patients who had thyroidectomies on our service had initial values for the serum iodine of 11.2, 11.8 and 18.6 micrograms respectively per hundred cubic centimeters.

5. Riggs, D. S., and Man, E. B.: A Permanganate Acid Ashing Micromethod for Iodine Determinations: I. Values in Blood of Normal Subjects, J. Biol. Chem. **134**:193, 1940.

6. Man, E. B.; Smirnow, A. E.; Gildea, E. F., and Peters, J. P.: Serum Iodine Fractions in Hyperthyroidism, J. Clin. Investigation **21**:773, 1942.

7. Man, E. B., and Peters, J. P.: Gravimetric Determination of Serum Cholesterol Adapted to the Man and Gildea Fatty Acid Method with a Note on the Estimation of Lipoid Phosphorus, J. Biol. Chem. **101**:685, 1933. Bogdanovitch, S. B., and Man, E. B.: The Effects of Castration, Theelin, Testosterone and Antuitrin-S on the Lipoids of Blood, Liver and Muscle of Guinea Pigs, Am. J. Physiol. **122**:73, 1938.

pressed phase of a manic-depressive condition. Iodine concentrations for the 17 manic-depressive patients in a depressed phase were not especially

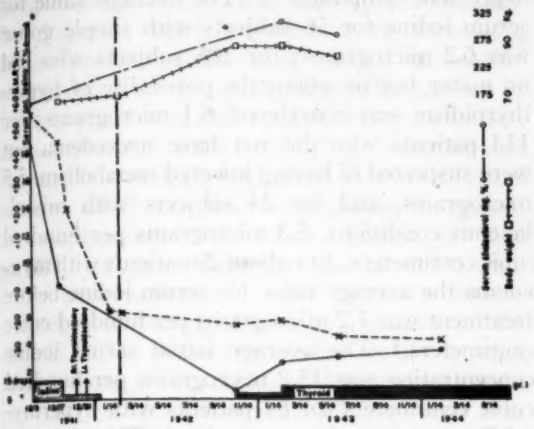

Fig. 2.—Clinical data on patient 1 before and after thyroidectomy.

Before therapy with strong solution of iodine U. S. P., a man aged 36 who had been in a hypomanic state for about two months, had a total serum iodine of 18.6 micrograms per hundred cubic centimeters. His basal metabolic rate could not be definitely established because of his tension, but it was between + 50 and + 60 per cent. His thyroid was enlarged; there was a definite tremor but no exophthalmos. His pulse rate was about 120 per minute. After therapy with strong solution of iodine U. S. P., the precipitable iodine of the serum fell to 8.5 micrograms per hundred cubic centimeters, and his basal metabolic rate, to + 20 per cent. A two stage thyroidectomy was performed. Clinical improvement was pronounced. Tension and anxiety decreased notably. While he was under treatment with the iodine solution, the clinical course, basal metabolic rate and serum iodine levels were typical of hyperthyroidism. Hyperplasia was recognized in the excised gland. There was a decided gain in weight after operation, and eleven months later the basal metabolic rate was — 23 per cent. The patient was given 0.5 grain (0.0325 Gm.) of thyroid daily, and after four months this was increased to 1 grain (0.065 Gm.). The patient has continued to take desiccated thyroid and has been able to conduct his business. He has had equivocal symptoms suggestive of mild depression.

low, but, with 2 exceptions, were between 4 and 6.5 micrograms per hundred cubic centimeters.

The values for serum iodine for 3 of the 17 patients of the second group, namely, the depressed patients whose conditions were not diagnosed as manic-depressive, were above the normal range. One of these 3 was the patient who had clinical signs of hyperthyroidism and underwent a thyroidectomy. The serum iodine values for the other 2 patients were between 8 and 9 micrograms per hundred cubic centimeters, a borderline range in which fall a few values for serum iodine of both normal subjects and patients with hyperthyroidism.

In figures 2, 3 and 4 the values for serum iodine and cholesterol, the basal metabolic rates and the body weights of the 3 patients with a clinical diagnosis of hyperthyroidism are shown graphically. The results of administration of strong solution of iodine U.S.P. before operation and of thyroid therapy after operation are also indicated in the figures. The first 2 manic-depressive patients were in a manic phase. After thyroidectomy the man was able to return to his business, and the woman, to her family and housekeeping. The third patient, who was not

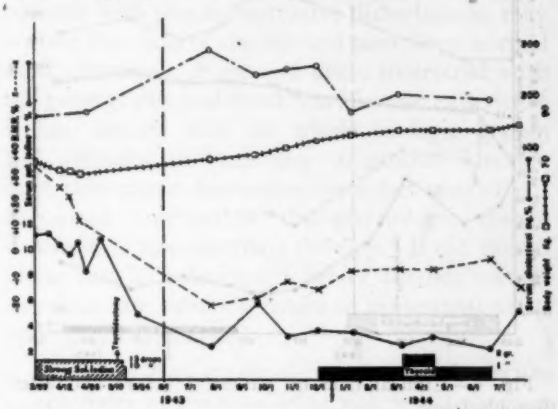

Fig. 3.—Clinical data on patient 2 before and after thyroidectomy.

A woman aged 32 who had shown moderate manic excitement of about three weeks' duration had a basal metabolic rate of + 33 per cent and a precipitable iodine content of the serum of 11.2 micrograms per hundred cubic centimeters. The patient had a diffusely enlarged thyroid, tachycardia, fine tremor, slight lid lag and warm, moist skin. Treatment with strong solution of iodine U. S. P. produced clinical improvement; the basal metabolic rate fell to + 12 per cent, and the precipitable iodine of the serum fell to 8.3 micrograms per hundred cubic centimeters and then rose again to 10.9 micrograms per hundred cubic centimeters. Subtotal thyroidectomy was performed, and examination of the excised gland revealed hyperplasia. After operation her weight increased; the basal metabolic rate fell to — 21 per cent, the precipitable iodine of the serum to 2.7 micrograms per hundred cubic centimeters and the serum cholesterol to 295 mg. per hundred cubic centimeters. The patient was given 1 grain of desiccated thyroid, then 2 grains (0.13 Gm.) for a short time and then 1 grain; at present she is not receiving any thyroid. At the time of writing, sixteen months after thyroidectomy, she is able to do her housework and care for her family. She is not manic or overactive. Insufficient time has elapsed to reveal whether thyroid medication should be resumed and continued.

manic-depressive, but had an agitated depression, was less tense and agitated after thyroidectomy, although her depression continued.

COMMENT

The observation that 22 of the 26 manic-depressive patients had serum iodine concentrations within the normal range supports the conclusion that manic and depressive conditions are not usually induced by abnormality in function of the thyroid gland. In fact, all the distinctly abnormal serum iodine concentrations in this series can be explained by the coincidence of a manic-depressive condition and overactivity or underactivity of the thyroid. The average serum iodine concentration for the 17 depressed patients of the manic-depressive group was 5.5

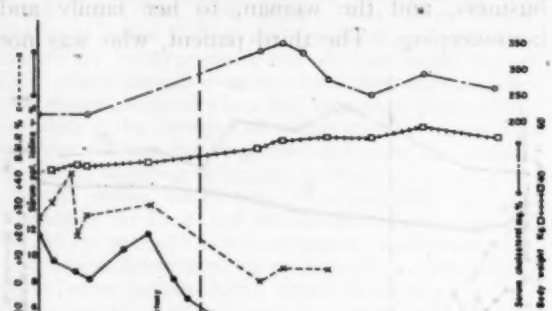

Fig. 4.—Clinical data on patient 3 before and after thyroidectomy.

A woman aged 53 with depression and agitation, which had begun about eighteen months before her admission to the hospital, had a firm nodule in the right lobe of the thyroid. She had a slight tremor but no exophthalmos. She had diabetes, which necessitated her taking about 10 units of regular insulin at the time of admission. The basal metabolic rate was initially only +25 per cent, but about two weeks later, after one week of treatment with a strong solution of iodine U. S. P., it was +42 per cent. The initial level of precipitable iodine in the serum of 11.7 micrograms per hundred cubic centimeters fell to 8.3 micrograms per hundred cubic centimeters after administration of the iodine solution was begun, and then rose again to 11.7 micrograms per hundred cubic centimeters. Thyroidectomy was not performed until seven weeks after treatment with strong solution of iodine U. S. P. was started because the patient's tension and anxiety persisted. The excised gland showed complete involution, with some degenerated adenomatous masses. After operation the anxiety and agitation diminished, but the depression continued. The serum total iodine fell to 3.1 micrograms per hundred cubic centimeters, and the serum cholesterol rose to 354 mg. per hundred cubic centimeters. Administration of ½ grain (0.0325 Gm.) of desiccated thyroid was started and was continued, without relief from the depression. Fifteen months after thyroidectomy the patient was transferred to a sanatorium.

micrograms; that for the 7 patients in a manic phase without hyperthyroidism, 6.1 micrograms, and that for the 16 depressed patients without hyperthyroidism who did not have a manic-depressive disturbance, 5.4 micrograms per hundred cubic centimeters. These averages agree closely with average values for patients without manic or depressive symptoms [2]: The average value for serum iodine for 56 subjects with simple goiter was 6.2 micrograms; for 105 subjects who had no goiter but in whom the possibility of hyperthyroidism was considered, 6.1 micrograms; for 113 patients who did not have myxedema but were suspected of having lowered metabolism, 5.5 micrograms, and for 24 subjects with miscellaneous conditions, 5.3 micrograms per hundred cubic centimeters. For about 29 patients with myxedema the average value for serum iodine before treatment was 1.2 micrograms per hundred cubic centimeters.[8] The average initial serum iodine concentration was 15.2 micrograms per hundred cubic centimeters for 84 patients with hyperthyroidism confirmed at operation.[2] This value of 15.2 micrograms per hundred cubic centimeters is an average one; some of the patients with hyperthyroidism have had initial serum iodine values as low as 9 micrograms per hundred cubic centimeters, while a few patients with mild hyperthyroidism have had serum iodine concentrations between 8 and 9 micrograms per hundred cubic centimeters.

The average serum iodine value of 5.5 micrograms per hundred cubic centimeters for all the depressed patients gives no indication of a relation between hypofunction of the thyroid and a depressive condition. Depressed patients do not present the whole picture of myxedema, which consists of edema, puffy skin, thin coarse hair, hoarse voice, low pulse rate, intolerance to low temperatures and anemia. The assumption that dysfunction of the thyroid is not related causally to the depressive syndrome is supported by the fact that administration of small amounts of desiccated thyroid did not influence the clinical course of patients with depressions. For example, the depression of patient 3, for whom data are presented in figure 4, was not influenced by the administration of desiccated thyroid. A patient with a mild depression, had been given 1½ grains (0.097 Gm.) of thyroid daily for some time. Thyroid therapy was terminated. Six weeks later the depression had not deepened. The values for precipitable iodine in the serum determined when administration of desiccated thyroid was stopped and, again, six weeks later were in the middle of the normal range, and the two values, 6.7 and 6.2 micrograms per hundred cubic centimeters respectively, agreed within the experimental error of the method.

These results seem to show that thyroid overactivity is not instrumental in bringing about a

manic condition. The average serum iodine for 7 manic patients was 6.1 micrograms per hundred cubic centimeters. Two patients with high levels of iodine in the blood had hyperthyroidism, the diagnosis being established by pathologic studies on the glands. The normal values for serum iodine of the manic-depressive patient in a manic phase who did not have hyperthyroidism are in contrast to the findings of Neustadt and Howard.[8] Although 9 patients is a small number on which to base conclusions, it should be emphasized that in a group of 250 to 300 patients determinations of the serum iodine were requested for those persons who were suspected of having abnormal function of the thyroid. The present evidence makes it most probable that the manic state of manic-depressive patients was associated with a high iodine concentration in the serum only in the occasional patients who, in addition, had hyperthyroidism.

A patient may have a manic-depressive disturbance and either hyperthyroidism or hypothyroidism at the same time; yet a manic-depressive disturbance is not necessarily related causally to abnormality in function of the thyroid. In figures 2, 3 and 4 have been presented data on 2 manic-depressive persons and on 1 depressed patient in whom hyperthyroidism and manic or agitated depressive conditions concurred. In all these patients thyroidectomy diminished the overactivity, tension and agitation. It is in the cases of such patients that the danger of not recognizing hyperactivity of the thyroid is paramount.

The incidence in manic and depressive patients of tremor and tachycardia, usually associated with hyperthyroidism; the concurrence of these two syndromes, and the amelioration after thyroidectomy of overactivity, tension and agitation suggest an occasional association of hyperthyroidism and manic-depressive states. Such an association occurs in other conditions; for example, in diabetes and in hyperthyroidism. An association between hyperthyroidism and manic-depressive states has been discussed by Moersch.[9] Their coincidence does not prove thyroid dysfunction to be a causal factor in manic-depressive disturbances. This coincidence is possible, although the function of the thyroid was normal in 22 of 26 manic-depressive patients, as shown by the serum iodine levels. In fact, one might question whether the manic-depressive condition may not play a causal role and induce hyperthyroidism in certain patients. For example, a history of previous episodes of depression in case 2 suggests that the manic-depressive condition was the underlying disturbance in this case. That hyperthyroidism occurred, although hypothyroidism was not observed in the present series of patients, makes one look for the cause of thyroid hyperfunction in these patients. Of course it is true that in any general series of patients studied consecutively, the incidence of hyperthyroidism is greater than the incidence of hypothyroidism. But if hyperthyroidism occurs in patients with manic-depressive disturbances, may not the function of the thyroid have been normal until the manic-depressive cycle interfered with the general physical condition? In our experience it has seemed that the whole biologic system has difficulty in returning to normal function once this manic-depressive cycle has started. If abnormal function of the physiologic system continues, more disorders develop. If the vicious circle can be interrupted before further trouble develops, the patient's return to his normal existence may be hastened.

Whether the manic-depressive state incites overactivity of the thyroid or not, it is important to remember that the two conditions are occasionally present together and are in no sense mutually exclusive. Although certain symptoms of the two disorders resemble each other, the patterns are different. Unless this is remembered, one or the other may be overlooked. The criteria for diagnosis of the two conditions are simply those for the diagnosis of each one separately. However, frequently in the presence of a manic-depressive condition two usual tests for hyperthyroidism are impracticable. The basal metabolic rate and its response to administration of iodine are not reliable. In these patients estimation of the precipitable iodine in the serum before and during administration of iodine has a peculiar value. Determinations of serum iodine would be of similar importance in cases of depression and hypothyroidism, although this combination seems to be a rarer one.

CONCLUSIONS

Thyroid function was evaluated by measurement of serum iodine concentration in 43 patients with manic or depressive disturbances. Of these, 26 patients had a manic-depressive disturbance and 17 a depressed but not manic-depressive condition.

8. Neustadt, R., and Howard, L. G.: Fluctuation of Blood Iodine in Cyclic Psychoses, Am. J. Psychiat. **99**: 130, 1942.

9. Moersch, F. P.: Psychic Manifestations Associated with Hyperthyroidism, Am. J. Psychiat. **91**:1215, 1935.

A clinical diagnosis of hyperthyroidism was made for 3 of the 43 patients. The values for the serum iodine of 36 of the remaining 40 patients fell within the normal range of 3 to 8 micrograms per hundred cubic centimeters.

Dysfunction of the thyroid cannot be considered as an essential factor in manic-depressive conditions or in manic overactivity or depressed underactivity. There is no way to prove or to disprove that occasionally disturbances of the thyroid may not participate in starting a manic-depressive cycle. In view of the fact that emotions affect the thyroid mechanism, it is conceivable, although the evidence is not yet conclusive, that manic-depressive disturbances may occasionally initiate imbalance of thyroid function.

Prof. John P. Peters and Dr. Alexander W. Winkler, of the Department of Internal Medicine, saw some of these patients in consultation and advised us in this investigation.

Yale University School of Medicine.

Abstracts from Current Literature

EDITED BY DR. BERNARD J. ALPERS

Physiology and Biochemistry

SALT METABOLISM IN POLIOMYELITIS. JAMES F. RINEHART, J. Nerv. & Ment. Dis. **99**:825 (May) 1944.

Rinehart investigated the possibility that a nonspecific factor lowering the immunity of the host might be responsible for the fact that during an epidemic of poliomyelitis relatively few persons are stricken with the disease. A group of cases of early poliomyelitis were studied with regard to chloride concentration of whole blood and of spinal fluid, packed volume of red blood cells and urinary output of chlorides under controlled intake of sodium chloride. It was found that depletion of chlorides and hemoconcentration were constant. The author believes that these findings represent a preexisting state favoring propagation of the virus and are not simply an effect of the illness. In support of the idea that depletion of salt may predispose to poliomyelitis is the summer incidence of the disease and the fact that often strong, robust children are affected. A history of physical overexertion prior to the onset is frequently present. These factors all lead to salt depletion and dehydration and may predispose to invasion and propagation of the virus of poliomyelitis.

CHODOFF, Langley Field, Va.

IMMEDIATE CIRCULATORY AND RESPIRATORY EFFECTS OF CONVULSIVE SHOCK. LAWRENCE F. WOOLLEY, J. Nerv. & Ment. Dis. **100**:64 (July) 1944.

Woolley reports on a study of the immediate effects on respiration and circulation of metrazol or electrical treatment preceded in each instance by a protective dose of curare, Determinations of the blood pressure and pulse rate were made before treatment, immediately after the injection of curare and every minute thereafter throughout the shock treatment until the values had become stabilized near the patient's norm. Ordinarily there is a considerable elevation in blood pressure and pulse rate prior to the start of the treatment, probably due to anticipatory apprehension. If the curare is not followed by shock, there is a tendency to a gradual fall toward normal over several hours. With deep curarization, there is a period of difficult breathing, and sometimes of stridor, but never respiratory distress or cyanosis. If the metrazol or the electrical current results in a petit mal seizure, a psychic equivalent or an apneic type of reaction, there occurs a fairly pronounced rise in both the blood pressure level and the pulse rate. With a grand mal convulsion, the systolic blood pressure rises during the latent period, reaches a peak during the tonic phase and then rapidly falls toward a normal level. Similar changes occur with the pulse rate. In the period of postseizure excitement there are marked irregularities in pulse rate and blood pressure. The depth of cyanosis occurring during the seizure depends directly on its duration and severity, the amount of mucus in the throat and the intensity of curarization. There is considerable variation in the circulatory and respiratory reactions in different patients and in the same patient during different treatments. It was found that extreme decreases in blood pressure, pulse rate or respiratory rate were promptly overcome by the administration of either epinephrine or neostigmine, thus suggesting that curare plays an important role in these accidents. The author feels that the marked changes in the blood pressure occurring during convulsive therapy may play an important part in bringing about the physical effects which result in postconvulsive confusion and memory defect and which probably contribute to the clinical improvement of the patient.

CHODOFF, Langley Field, Va.

REACTIONS OF MONKEYS OF VARIOUS AGES TO PARTIAL AND COMPLETE DECORTICATION. MARGARET A. KENNARD, J. Neuropath. & Exper. Neurol. **3**:289 (July) 1944.

Kennard reports her observations on the reactions of monkeys following the removal of extensive portions of the cortex. Twenty-five Macaca mulatta monkeys were used, of which 18 were infants of dated birth in the first few months of life and 7 were either immature or adult animals. Only 4 of these animals were totally decorticated; but 12 of the remaining 21 were deprived, by cortical operation, of all "voluntary" motor power. The remaining 9 monkeys served as controls.

Kennard reports that the decorticate adult Macaca has a motor performance limited to the simpler righting reflexes which alter the posture of its extremities as its position in space is changed. It is moderately spastic and relatively less motile than the decorticate infant. The latter is able to right itself, to maintain a standing posture and to walk spontaneously. Activities such as sucking, swallowing, vocalizing or clinging are more complex and less stereotyped than those of the adult. Spasticity is absent, and the posture at rest is one of exaggerated flexion.

It is clear that removal of the frontal association areas, areas 8, 6 and 4, the parietal areas and the basal ganglia from infant monkeys has some effect on reactions in infancy. The observations indicate the presence of some cortical function at an early age. The infant cortex has a greater capacity for reintegration of motor activity than has the cortex of the adult Macaca. Also, reorganization of the cortex injured in infancy follows a pattern which is fixed both by the age of the animal and by the size and site of the lesion.

GUTTMAN, Philadelphia.

THE MECHANICS OF TRAUMA WITH SPECIAL REFERENCE TO HERNIATION OF CEREBRAL TISSUE. A. H. S. HOLBOURN, J. Neurosurg. **1**:190 (May) 1944.

On the assumption that the brain behaves like an elastic body, Holbourn attempts to establish a theory for the pathogenesis of traumatic cerebral cysts. He introduces his thesis by establishing the basic concepts of the theory of elasticity: 1. Stress means force per unit area. 2. Strain is the displacement of a body as a consequence of stress. 3. Hydrostatic pressure (e. g., intraventricular cerebrospinal fluid pressure) is a simple type of stress. 4. A force acting tangential to a surface is a shearing stress, and its resultant strain is a distortion of the object to which the stress is applied (unlike hydrostatic pressure).

The foregoing theory may be applied to inanimate matter: If enough stress is applied to a substance, that substance will not recover its original shape from the resultant distortion strain; i. e., elastic resilience fails when the shearing stress exceeds a certain critical value. By a priori reasoning, the author applies the theory of elasticity to the brain, which he regards as similar to inanimate matter. If the stress only slightly exceeds the critical value, a cerebral "crack" occurs, with repair by glial scarring. If the stress is high, there is a greater liability for the increased distortion to produce a cerebral cyst; i. e., the cerebral tissues are torn apart.

Lastly, the author applies the theory of elasticity to herniation of the brain through an opening in the skull due to intraventricular pressure. He demonstrates the appropriateness of the application by using a photoelastic gelatin model. He was able to predict the positions and shapes of the injured regions of the brain, and his predictions were found to coincide with the actual pathologic changes observed by other investigators.

WHITELEY, Philadelphia.

Diseases of the Brain

TRAUMATIC PNEUMOCEPHALUS WITH SPONTANEOUS VENTRICULOGRAMS. ABRAHAM KAPLAN, J. Neurosurg. **1**:166 (May) 1944.

Cerebrospinal rhinorrhea with pneumocephalus may have various causes but usually is secondary to fracture of the posterior wall of the frontal sinus or the cribriform plate of the ethmoid bone. Through a tear in the adjacent meninges air enters the subarachnoid space; it may become trapped in the subdural, subarachnoid or ventricular spaces, or even in the brain substance. Meningitis is the most serious complication. Treatment consists of rest, dependent posture, decrease in intracranial pressure, administration of sulfonamide compounds and surgical repair when needed.

The author reports a case in which rhinorrhea appeared after twenty-nine days and spontaneous pneumoventriculograms were obtained.

WHITELEY, Philadelphia.

EXPERIMENTAL TRAUMATIC CEREBRAL CYSTS IN THE RABBIT. MURRAY A. FALCONER and DOROTHY S. RUSSELL, J. Neurosurg. **1**:182 (May) 1944.

Beneath the center of experimental decompression areas in rabbit skulls, 50 per cent of the brains showed pathologic changes in the subcortical white matter, and 30 per cent, cyst formation. Edema, hemorrhages, softening and cavitation all usually appeared within one week after operation. At the end of two to seven weeks the walls of the cysts had become lined with glia. At the medial lip of the artificially produced herniation of the brain, a scar usually extended from the wall of the cyst to the surface of the brain.

The authors conclude that all these changes have a structural basis, since they always occured at or just beneath the junction of the cortex and the white matter; that is, lines of cleavage during physical strains result at the sites of transition in tissue consistencies. But splitting of tissues must always be preceded by certain pathologic changes, with resultant softening of the brain.

The authors believe these studies may have some bearing on the pathogenesis of traumatic cerebral cysts in man.

WHITELEY, Philadelphia.

RUPTURE OF A LEFT TEMPOROSPHENOIDAL BRAIN ABSCESS INTO THE VENTRICLE. LOUIS E. WOLFSON, New England J. Med. **230**:170 (Feb. 10) 1944.

Wolfson reports the case of a 56 year old man who had chronic infection of the left mastoid for fifty-one years. After an acute infection of the upper respiratory tract, an exacerbation of the mastoiditis developed, and a radical mastoidectomy was performed on that side. Sulfadiazine therapy was given. Cultures of pus from the mastoid area revealed Staphylococcus albus and a nonhemolytic streptococcus.

Five days after operation right hemiparesis and stupor developed. The mastoidectomy wound was reexplored, and the underlying dura was found to be tense. The dura was incised, as was the brain, and a cannula was inserted for a distance of 3 cm., when pus was obtained (Staph. aureus, diphtheroids and a nonhemolytic streptococcus). Clinical recovery was prompt, and the level of sulfadiazine in the blood was maintained at about 10 mg. per hundred cubic centimeters.

Subsequently, iodized poppyseed oil was injected into the cavity of the abscess, and roentgenograms indicated that it communicated with the left lateral ventricle.

Wolfson states that the use of a high concentration of sulfadiazine probably checked further spread of the infection. Rupture of such an abscess is extremely rare and is generally seen only at autopsy. Roentgenograms showing such an event during life have not heretofore been reported on.

GUTTMAN, Philadelphia.

APPERCEPTIVE BLINDNESS IN LISSAUER'S DEMENTIA PARALYTICA. MARY T. PATTERSON and E. STENGEL, J. Neurol. & Psychiat. **6**:83 (July-Oct.) 1943.

Patterson and Stengel report a case of Lissauer's dementia paralytica in which apperceptive blindness was a prominent feature and was correlated anatomically with accentuation of the paretic changes in the parastriatal areas of the occipital cortex. The authors interpret the apperceptive blindness as a reaction of denial of chaotic visual impressions of the outer world, resulting from interaction of a severe thought disorder, lack of attention, inability to focus and visual agnosia. The psychologic mechanisms underlying apperceptive blindness are similar to those of Anton's symptom of unawareness of cortical blindness, and both have much in common with psychoneurotic symptoms.

MALAMUD, Ann Arbor, Mich.

TRAUMATIC DILATATION OF THE CEREBRAL VENTRICLES. D. W. C. NORTHFIELD, J. Neurol. & Psychiat. **7**:1 (Jan.-April) 1944.

Traumatic dilatation of the ventricles may be divided into three types: (1) local bulging, resulting from focal contusion of the brain; (2) enlargement of the whole of one lateral ventricle, either ipsilateral or contralateral to the site of injury, and (3) general symmetric enlargement of both lateral ventricles. Northfield discusses the possible mechanisms involved in the last two forms. These types of ventricular dilatation may result either from disturbances in the cerebrospinal fluid system or from atrophy of the brain tissue. The former may arise from excessive production, delayed circulation or impaired absorption of the cerebrospinal fluid. While excessive production due to injury is improbable, there are clinical and histologic evidences that block in the cerebrospinal fluid system leads to occlusion of

the leptomeningeal spaces, scarring of the cortex and resulting dilatation of the ventricles. The weight of evidence, however, indicates some change occurring primarily in the brain tissue which leads to atrophy and in this way to hydrocephalus ex vacuo. Generalized cerebral edema has not yet been proved to be a cause of such atrophy. A number of observations suggest that in cases of severe trauma a temporary excessive outpouring of fluid from the choroid plexus takes place. Through transient delay of circulation and absorption, due to the presence of blood and a traumatized ependyma, this fluid penetrates the wall of the ventricle and passes into the brain tissue; there, by impairing its nutrition, it leads to edema and ultimately to gliosis and atrophy.

N. MALAMUD, Ann Arbor, Mich.

CONGENITAL CYST IN THE LEFT TEMPORAL LOBE. S. OBRADOR, F. PASCUAL DEL RONCAL and M. FALCÓN G., Arch. de neurol. y psiquiat. de Mexico **6**:385 (Sept.-Oct.) 1943.

A 27 year old woman complained of persistent frontal and occipital headache and recurrent attacks of vertigo, of five months' duration. There were a few attacks of transitory blurring of vision. A lumbar puncture made soon after the onset relieved her symptoms for one month. Occasionally she felt as though her limbs did not exist. Loss of consciousness, without convulsive movements, occurred once.

Examination showed bilateral papilledema, right homonymous hemianopsia, weakness of the lower right side of the face, a tendency to veer to the left in the Romberg position and some inward drift of the outstretched right upper limb. The patient showed mild euphoria, some intellectual enfeeblement and amnestic aphasia. There were abnormally slow waves (4 to 5 per second) of low voltage in the left temporo-occipital region and a few delta waves in the right frontal area. Pneumoencephalographic examination showed that the right ventricle was enlarged and displaced to the right and that a small amount of air was present in the posterior portion of the left ventricle, which seemed to be pushed upward and backward.

Operation showed a voluminous cyst with white, smooth walls and poor vascularization, in the subcortex of the left temporal lobe. The cyst was more than 6 cm. in diameter and was filled with cerebrospinal fluid. No tumor nodules were found. Biopsy of a small piece revealed the wall of a cystic cavity lined with ependyma; there were a few amyloid bodies and mild neuroglial proliferation in the wall. The authors consider that this cyst was congenital and that at one time it was connected with the wall of the lateral ventricle.

SAVITSKY, New York.

Diseases of the Spinal Cord

CHORDOMATA: A REVIEW OF THE LITERATURE, WITH REPORT OF A SACROCOCCYGEAL CASE. DANIEL B. FAUST, HUGH R. GILMORE JR. and CHARLES S. MUDGETT, Ann. Int. Med. **21**:678 (Oct.) 1944.

Faust, Gilmore and Mudgett review the literature of chordomas and report an additional case. The survey indicates the following distribution of recorded lesions: cranial, including spheno-occipital and nasopharyngeal, 92; vertebral, 34; caudal or sacrococcygeal, 122, and others, 4. Thus, 48.4 per cent of the reported lesions were in the sacrococcygeal region and 36.5 per cent in the cranial region. With few exceptions, most of the remaining 15.1 per cent of the lesions were located along the vertebral column.

The signs and symptoms of cranial chordoma are those of any intracranial neoplasm or of a tumor of the nasopharyngeal cavity. Chordomas involving the vertebral or the sacrococcygeal region do not produce symptoms or signs which differ from those of any other neoplasm. The lesions may be relatively benign but are more frequently malignant, with or without metastases. Successful surgical removal depends on the location and the size of the lesion. Both roentgen and radium therapy are of questionable value. A fatal termination in the course of one to six years is the rule, but cures following surgical intervention have been reported.

Faust, Gilmore and Mudgett report the case of a 23 year old Negro who had a large sacrococcygeal chordoma, extending into the right lower quadrant of the abdomen, with extensive pulmonary and adrenal metastases.

GUTTMAN, Philadlephia.

PATHOLOGY, CLINICAL MANIFESTATIONS AND TREATMENT OF LESIONS OF THE INTERVERTEBRAL DISKS. ALBERT OPPENHEIMER, New England J. Med. **230**: 95 (Jan. 27) 1944.

Oppenheimer reports on the pathologic process, clinical manifestations and treatment of lesions of the intervertebral disks. He observed 826 patients with lesions of disks, a control series of 200 persons without symptoms and another control series of 100 patients with complaints suggestive of such lesions. An attempt was made to correlate the clinical and anatomic findings and to evaluate various methods of management and treatment of these lesions.

The author concludes that the high incidence of lesions of the disks may be explained by the evolutionary development of the human spine. The system of bones and joints, originally adapted to bear almost no vertical stress, sustains in man the whole impact of the upright posture and locomotion. Regardless of the cause of flattening of the intervertebral disk, narrowing of the corresponding intervertebral spaces results, associated with displacement of articular processes, narrowing of the neural foramen and abnormal contact between vertebral bodies.

The clinical manifestations depend on the anatomic changes described rather than on the degree of thinning of the disk. Narrowing of the neural foramen may induce radicular pain, but compression of the nerve roots does not always occur, owing to the variable relationship between the caliber of the nerve and the degree of impingement. Pain in the back and limitation of vertebral movements are less frequent (about 20 per cent) and seem to be caused predominantly by involvement of the apophysial joints as a result of a lesion of an intervertebral disk. In most cases lesions of disks produce symptoms felt in the limbs, and not in the back or neck.

The signs and symptoms of radicular neuralgia and neuropathy are often indistinguishable from those of myalgia, arthritis, bursitis and referred visceral pain. The differential diagnosis can be made only after exhaustive clinical survey.

Oppenheim states that surgical removal of a ruptured disk followed by spinal fusion did not always prevent the development after several years of symptoms caused by subsequent thinning of the disk. Conservative treatment yielded satisfactory results in about 75 per cent of cases.

GUTTMAN, Philadelphia.

MYELITIS DUE TO VACCINATION. G. J. DIXON, J. Neurol. & Psychiat. **7**:18 (Jan.-April) 1944.

Dixon reports the case of a man aged 27 who had fever, muscular pain and unsteadiness of gait nine days after primary vaccination. After a temporary remission, there was sudden onset of paraplegia on the twenty-third day after vaccination. There was gradual and almost complete recovery in six months. The case differs from cases of classic postvaccinal encephalitis in that the symptoms were spinal rather than cerebral.

N. MALAMUD, Ann Arbor, Mich.

BRACHIAL PAIN FROM HERNIATION OF CERVICAL INTERVERTEBRAL DISC. F. A. ELLIOTT and MICHAEL KREMER, Lancet **1**:4 (Jan. 6) 1945.

Elliott and Kremer report 8 cases of brachial pain caused by herniation of the sixth cervical intervertebral disk. The pain was in the back of the shoulder, down the back of the arm and along the radial border of the forearm and sometimes in the upper pectoral region. There were paresthesias in the thumb and the index and middle fingers. In some cases there was a history of acute stiff neck. The signs include limitation of movement of the neck; pain produced in the arm by movements of the neck and by downward pressure on the head, and tenderness, weakness and wasting of the pectoralis major, triceps and extensor muscles of the wrist and fingers. The triceps jerk was reduced or absent, and there was usually hypalgesia over the thumb and the index finger.

The clinical picture was that of a lesion of the seventh cervical root. Trauma was not an essential precursor of the syndrome, and even when present it was often of minor degree. Myelographic examination with a contrast medium in 3 cases showed a filling defect opposite the sixth intervertebral disk, involving the seventh cervical root on the affected side. Treatment was conservative. However, the authors conclude that if conservative measures of fixation and traction of the head do not succeed in eliminating the pain surgical intervention is indicated.

YASKIN, Camden, N. J.

Peripheral and Cranial Nerves

MULTIPLE PERIPHERAL NEURITIS OCCURRING WITH SULFONAMIDE THERAPY. M. A. BLANKENHORN, Ann. Int. Med. **20**:423 (March) 1944.

Blankenhorn found multiple peripheral neuritis in 6 of a total of 600 patients who were given sulfonamide therapy. Three of the patients had chronic alcoholism, and a fourth was thought to have the condition. Three patients gave a history of a poor diet and showed evidence of hypovitaminosis.

Blankenhorn also reported on 8 patients who presented evidence of neuritis before a sulfonamide drug was administered. In this group, only 1 patient's symptoms became more pronounced after the sulfonamide therapy. The author concludes that the administration of vitamins may have prevented the neuritis from becoming aggravated.

GUTTMAN, Philadelphia.

TONSILLECTOMY AND POLIOMYELITIS: ONE CASE OF POLIOMYELITIS FOLLOWING 8,915 TONSILLECTOMIES. JOHN RANDOLPH PAGE, Arch. Otolaryng. **39**:323 (April) 1944.

Page obtained data from the department of health of the city of New York showing the number of cases of poliomyelitis that occurred in the five years from 1937 to 1941 inclusive. The disease was most prevalent in 1937, 1939 and 1941, the number of cases during those years being 243, 184 and 404, respectively. All patients who had undergone tonsillectomy in the Manhattan Eye, Ear, Nose and Throat Hospital during these three years were communicated with by mail. A total of 27,849 postal cards were sent out, with a return card attached. Two questions were asked: 1. Have you had any illness since the tonsillectomy? 2. What were the nature and date of illnesses, if any?

A total of 8,915 replies were obtained, and among them 1 case of poliomyelitis was reported. The case occurred in a 7 year old boy about one month after his tonsils and adenoids had been removed.

RYAN, M.C., A.U.S.

SUTURELESS REUNION OF SEVERED NERVES WITH ELASTIC CUFFS OF TANTALUM. PAUL WEISS, J. Neurosurg. **1**:219 (May) 1944.

The following advantages in linking severed nerve stumps with closely fitting sleeves appear to be attained. 1. Absence of sutures permits nerve fibers to regenerate in a strictly longitudinal direction and avoids the formation of adhesions due to tissue reaction. 2. Dissipation of fluid necessary for nerve regeneration is prevented. 3. Adhesions between the nerve junction and the surrounding tissues are prevented.

Weiss has devised a method whereby normally unelastic tantalum foil can be annealed to the elasticity and resilience necessary to form it into tight, permanent wound sleeves. These sleeves are closely fitted around the approximated nerve ends, and the aforementioned advantages are attained.

Eleven experimental animal unions were assayed, with 9 good results from an anatomic viewpoint. The functional results will be reported later.

WHITELEY, Philadelphia.

ELECTROMYOGRAPHIC STUDIES OF MUSCLE DYSFUNCTION IN INFECTIOUS POLYNEURITIS AND POLIOMYELITIS. MARY A. B. BRAZIER, ARTHUR L. WATKINS and ROBERT S. SCHWAB, New England J. Med. **230**:185 (Feb. 17) 1944.

Brazier, Watkins and Schwab studied 10 cases of infectious polyneuritis (so-called Guillain-Barré-Strohl syndrome) and compared the findings with those in a similar number of cases of poliomyelitis and of traumatic nerve lesions. The authors conclude that their studies revealed the following similarities of muscle dysfunction in infectious polyneuritis and poliomyelitis: Muscular tenderness and paresis were characteristic of both diseases, and the electrical abnormalities in both conditions were correlated with weakness rather than with "sensitivity." Partially paralyzed muscles showed hyperirritability when stretched; this was relieved by hot fomentations. The authors conclude that paretic muscles are hyperirritable even when at rest, with discharging electrical potentials characteristic of regenerating motor units. Reciprocal innervation was frequently disrupted in cases of polyneuritis and poliomyelitis, with consequent simultaneous activation of opposing muscles. This phenomenon was attributed to pain, associated with activity or motion.

The disorganization of reciprocal innervation was not so marked in the cases of polyneuritis because the

simultaneous activation of opposing muscles in this disease was not characterized by synchrony of component discharge.

GUTTMAN, Philadelphia.

POST-TRAUMATIC PAIN AND THE CAUSALGIC SYNDROME. J. DOUPE, C. H. CULLEN and G. Q. CHANCE, J: Neurol. & Psychiat. **7**:33 (Jan.-April) 1944.

The causalgic syndrome is characterized by persistent severe pain in the hand or foot following an injury to a limb despite the absence of apparent cause. Pain is the central feature of the syndrome, while nutritional disturbances in the form of changes in the skin or osteoporosis of the bones may or may not be associated. The authors are of the opinion that causalgic pain is due to the activation of sensory fibers by efferent impulses in the sympathetic fibers. This view is based on the following facts: 1. The pain is spontaneous, the result of alternating activities of sudomotor and vasoconstrictor fibers; it is thus related to the needs of thermoregulation rather than to any external or local influence. 2. The pain is diffuse and is described as hot and burning because the small fibers for pain and temperature sensation are sensitive to the action currents of the sympathetic fibers. 3. Emotional excitement or stimulation aggravates the pain because of the associated discharge in sympathetic fibers. 4. A tendency to profound mental changes exists. 5. The causalgic pain is relieved by sympathetic block. This theory also serves to explain the increased blood flow in the painful limb, since stimulation of afferent fibers causes antidromic vasodilatation, while the changes in the skin are caused by vasodilatation and disuse.

On the basis of these principles, the authors report a series of cases illustrating three types of post-traumatic pain: (1) psychogenic, (2) causalgic and (3) dystrophic. The results of therapeutic test, together with other neurotic features, serve to distinguish the psychogenic from the other types. The causalgic type may be further classified as proximal or distal, depending on whether the pain originates at the site of the nerve lesion or near the termination of the fibers, the distal form being due to edema or ischemia. Dystrophic pain is secondary to disturbances of nutrition resulting from such factors as disuse, defective arterial supply and defective venous or lymphatic drainage.

MALAMUD, Ann Arbor, Mich.

Treatment, Neurosurgery

REHABILITATION OF THE NERVOUS SYSTEM IN WAR TRAUMA. A. R. LURIA, Am. Rev. Soviet Med. **2**:44 (Oct.) 1944.

Luria bases his observations on the work at the neurosurgical rehabilitation clinic of the All-Union Institute of Experimental Medicine and the Convalescent Hospital. The problem of rehabilitation is to direct and organize functional recovery. Rehabilitation becomes an independent branch of medicine, having its own rationale and requiring its own methods.

Of all war casualties, 8 per cent involve nerve injuries. Their importance lies in the severity and extent of functional damage. Luria stresses the fact that functional recovery is not always hopeless, and study reveals that specific treatment may help the patient regain impaired function, even partially, without waiting for nerve regeneration to be completed. Functional disturbance after nerve injury is produced by at least two components: (1) local nerve palsy and (2) associated inhibition of a functional nerve aggregate. Surgical intervention is the first step in rehabilitation.

Luria states that the training of isolated muscle groups through various mechanotherapeutic measures, gymnastics and motor stimulation by galvanotherapy are insufficient for rehabilitation. Experience at the Convalescent Hospital shows that directed objective movements, and not isolated mechanical ones, possess the necessary organizing function. The leading place in a system of rehabilitation therapy for peripheral nerve palsy must be occupied by planned work or by occupational therapy. The planned movements depend little on specific muscles and can be executed by various combinations of other muscle groups. Instruments especially adapted to injured hands were made in the recovery clinic. The most successful results were obtained when the tool was modified to accommodate improvements and to stimulate further activity on the part of the injured extremity.

Rehabilitation following injuries to the brain is based on the "transference of function" to another system, e. g., the substitution of touch for sight or the use of the good hand for that of the paralyzed one. "This 'substitutive' compensation requires directed and prolonged exercises, to train new nerve centers for precise work." However, this shift is not the only therapeutic measure for the treatment of cerebral injuries. The complex function of the brain is to some extent as independent of separate fixed cerebral areas as is planned movement of any single muscle. By location of an impaired functional link and by substitution of a new one, recovery is instituted.

Luria concludes that damage to the brain does not necessarily lead to a hopeless functional defect. Every act follows a certain pattern, and the functional system is remarkable for its considerable plasticity. This is the basis for reconstruction therapy. In many instances, defects arising from war trauma are overcome, and the patient regains, to some degree, his lost working capacity.

GUTTMAN, Philadelphia.

MIGRAINE HEADACHES RELIEVED BY HYPOGLYCEMIC REACTION. SIDNEY J. TILLIM, Ann. Int. Med. **20**:597 (April) 1944.

Tillim reports 2 cases in which the patients were treated for migraine with injections of ergotamine tartrate, inhalations of pure oxygen or oxygen and 7 per cent carbon dioxide, intravenous injections of thiamine hydrochloride, histamine desensitization and administration of various glandular preparations, with little or no success. Both the patients became addicted to opiates. The author observed that intravenous injections of insulin promptly and fully aborted the migraine attacks which occurred during hospitalization. He states that induced hypoglycemia is antispasmodic and antagonistic to sympathetic activity and concludes that this action relieved the headaches.

GUTTMAN, Philadelphia.

A PRELIMINARY REPORT ON A METHOD FOR LENGTHENING THE EFFECT OF A SYMPATHETIC NERVE BLOCK. FERDINAND C. LEE, DAVID I. MACHT and ROSS Z. PIERPONT, Bull. Johns Hopkins Hosp. **74**:119 (Feb.) 1944.

Lee, Macht and Pierpont report on a method for prolonging the effect of a sympathetic nerve block. Paravertebral injections of 10 cc. of peanut oil containing 4 per cent monobromohydroxybenzyl alcohol were given 26 elderly patients with arteriosclerosis. In 24 patients

the temperature of the foot did not increase until three hours after the injection, and then the limb remained warm for about five days. At the end of eight days the beneficial effect disappeared. In 1 patient the total effect persisted about four days, while in the remaining patient no response was noted.

The method was developed primarily to avoid the almost daily injections for the treatment of thrombophlebitis, but the authors believe that it may prove helpful in any case in which improved circulation in the extremities is required. GUTTMAN, Philadelphia.

THE EXCRETION OF PENICILLIN IN THE SPINAL FLUID IN MENINGITIS. DAVID H. ROSENBERG and J. C. SYLVESTER, Science **100**:132 (Aug. 11) 1944.

Rosenberg and Sylvester administered penicillin in doses of 20,000 to 40,000 Oxford units intravenously and intramuscularly to 8 patients with meningitis. For 6 of these patients the condition had been proved to be meningococcic meningitis. Sixty to one hundred and forty minutes after administration penicillin was recovered from the cerebrospinal fluid, following lumbar puncture, in concentrations of 0.03 to 0.35 unit per cubic centimeter.

These data suggest that penicillin administered intravenously or intramuscularly in adequate doses may be effective in the treatment of meningitis without supplementary intrathecal therapy.

GUTTMAN, Philadelphia.

PROSTIGMINE AND EPHEDRINE IN MYASTHENIA GRAVIS. A. WILSON and H. B. STONER, Lancet **1**:429 (April 1) 1944.

Wilson and Stoner treated a series of 10 patients with parenteral injections of neostigmine methylsulfate and oral administration of neostigmine bromide, given alone or with ephedrine. Ephedrine given alone, either orally or subcutaneously, was also tried. Their results supported the observations in previous work in demonstrating that patients treated with the two drugs together gave more prolonged clinical responses than patients treated with neostigmine alone. "In all cases combined parenteral administration increased the degree and duration of relief from symptoms." The addition of ephedrine was particularly effective in alleviating diplopia and asthenia; in some cases ergographic records confirmed the latter effect, and often the patients themselves volunteered the information that they felt an increase in general muscular strength. Ephedrine given alone helped only 1 patient to any degree.

The cholinesterase activity of the serum was studied, and its inhibition during treatment was found to parallel, but not necessarily to equal in degree, the clinical change. The authors felt that the extra benefit derived from taking ephedrine could not be attributed to a change in cholinesterase activity alone.

The clinical effects of neostigmine were attributed both to the neutralization of a substance circulating in the blood which produces a partial block in neuromuscular transmission and to the inhibition of cholinesterase activity. The extra benefit derived from ephedrine when given with neostigmine was thought to be gained through prolongation of an epinephrine effect. Whether that effect takes place by augmenting "the action of acetylcholine protected by prostigmine, or whether adrenaline potentiates the anti-curare action of prostigmine is a question which can be settled only by further investigation." McCARTER, Philadelphia.

Encephalography, Ventriculography, Roentgenography

NORMAL AIR ENCEPHALOGRAMS IN PATIENTS WITH CONVULSIVE SEIZURES AND TUMOR OF THE BRAIN. H. HOUSTON MERRITT and CHARLES BRENNER, New England J. Med. **230**:224 (Feb. 24) 1944.

Merritt and Brenner report the histories of 3 patients (38, 27 and 19 years old) who suffered from convulsive seizures and had normal pneumoencephalograms seven, twenty and thirty months, respectively, after their first convulsion. A cerebral tumor was subsequently found in each case. All the tumors were astrocytomas—1 in the left temporal lobe, 1 in the right motor area and 1 in the right frontal lobe.

The authors conclude that although cerebral tumor is among the rarer causes of convulsive seizures, such a tumor may cause convulsive seizures without producing any demonstrable distortion of the ventricular system. A cerebral tumor is not likely to produce any change in the ventricular system unless it is large enough to produce focal neurologic signs or signs of increased intracranial pressure. If, in the absence of these signs, it is decided that an air study is advisable, a negative report should not be accepted as conclusive proof that no tumor is present. GUTTMAN, Philadelphia.

SOME CONSIDERATIONS CONCERNING THE ROENTGEN DIAGNOSIS OF SKULL FRACTURES. J. C. KENNING and IVOR D. HARRIS, Radiology **41**:532 (Dec.) 1943.

Kenning and Harris review 9,000 roentgenograms revealing fracture of the skull. Four routine exposures were made: two lateral views and a frontal and an occipital view. Additional exposures were made in questionable cases.

The fractures were divided into three groups: (1) those in the anterior third of the skull, involving the frontal area; (2) those in the middle third, involving the parietal, sphenoid, temporal and mastoid area, and (3) those in the posterior third, involving the occipital bone. Of the fractures, 26.8 per cent were in the anterior third, 45.3 per cent were in the middle third and 27.9 per cent were in the posterior third.

Roentgenographic differentiation of linear fractures from suture lines, diploic markings, vascular grooves and artefacts is often difficult. Sometimes only by careful study is the differentiation made. Fractures of the middle third are the most easily missed.

Complicating fractures of the anterior third include involvement of the cribriform plate of the frontal sinus, with an occasional aerocele, and involvement of the optic foramen. In the middle third, one may see involvement of the sphenoid sinus and the mastoid. Bony nonunion of fractures of the mastoid may persist indefinitely. Involvement of the foramen magnum may be seen with fractures of the posterior third.

TEPLICK, Philadelphia.

TABETIC ARTHROPATHY OF THE HIP. IRVING WALIN, Radiology **42**:79 (Jan.) 1944.

Walin reports a case in which neurogenic arthropathy (Charcot joint) was followed from its incipiency.

A white woman aged 57 had the original roentgenograms made because of dislocation of the left hip. Postreduction roentgenograms revealed that the hip joint was normal. Seven weeks after reduction the

hip again became dislocated, without trauma. A brace was applied. Roentgenograms made seven months after the original dislocation revealed extensive ossification of the joint capsule. Five months later another spontaneous "slipping" occurred. Roentgenograms at this time revealed typical neurogenic arthropathy with disruption of the head and fragmentation. The proximal head of the femur was dislocated superiorly.

TEPLICK, Philadelphia.

KLIPPEL-FEIL MALFORMATION. WILLIAM E. ALLEN JR., Radiology **44**:79 (Jan.) 1945.

The Klippel-Feil anomaly is characterized by absence or shortening of the neck, lowering of the hair line and limitation of motion of the neck, especially lateral bending. All or most of the cervical vertebrae may be fused. A large number of associated anomalies and deformities of the cervical vertebrae are commonly seen.

The author reports a case of this anomaly in a 24 year old soldier, whose sole complaint was a small tumor on the right shoulder which caused him some difficulty in carrying a pack. The following fifteen deformities and anomalies were seen in the roentgenograms: (1) elevation of the right scapula; (2) fusion of the first cervical vertebra and the occiput; (3) fusion of the bodies of the second and third cervical vertebrae; (4) fusion of the spinous processes of the second and third cervical vertebrae; (5) narrowing of the body of the fourth cervical vertebra; (6) spina bifida occulta of the bodies of the fourth and seventh cervical vertebrae; (7) bifid spinous process of the fifth cervical vertebra; (8) partial fusion of the bodies of the seventh cervical and first dorsal vertebrae; (9) dorsal hemivertebra; (10) deformed bodies of the upper dorsal vertebrae; (11) kyphosis and scoliosis of the dorsal portion of the spine to the right; (12) right cervical rib; (13) fusion of the first and the second rib on the right; (14) rudimentary right twelfth rib, and (15) thinning of the left fifth rib posteriorly.

TEPLICK, Washington, D. C.

Society Transactions

ILLINOIS PSYCHIATRIC SOCIETY

DAVID SLIGHT, M.D., *President*

Regular Meeting, May 6, 1944

Group Psychotherapy in Mental Institutions. DR. J. W. KLAPMAN, Chicago,

An important instrument of treatment fast emerging into general use wherever large number of patients are being cared for is the practice of group psychotherapy.

Its therapeutic effects are mediated largely through the influence of group emotion and group formation, and one of the first clear expositions of this group emotion was given by Freud, in his "Mass Psychology and the Analysis of the Ego." Freud confined himself to one type of group formation—that in relation to a leader. Redl amplified the subject and showed that group emotion may crystallize about a person who could in no sense be regarded as the leader; it may even crystallize about a person outside the group. Redl called such a person—the focus of group emotion —"the central person," but not necessarily its leader. In this there is no fundamental conflict between Freud and Redl, but the latter has expanded and amplified the range of group emotional factors.

In group psychotherapy the author finds predominantly active as group emotional formation a combination in various degrees of three types of Redl's group formations: (1) the patriarchal sovereign type, (2) the leader type, the group formation corresponding most closely to Freud's conception, and (3) the tyrant type.

The types described by Redl do not represent the whole possible range of group formations but are a few samples. As samples, they are described in more or less "pure culture." In the actual practice of group therapy one finds elements of these formations occurring in various combinations, depending on the personality of the therapeutist, the character of the group and any special circumstances surrounding the therapy. If the therapeutist becomes too stringent in his supervision, there is a melting away of spontaneity. If he is too permissive and narcissistic, drives become overtly manifest, interest will lag and group formation of utilizable transferences will be sensibly impaired. But under favorable conditions there is a perceptible transference to the therapeutist and from patient to patient because there is emotional acceptance, more or less, of interpretations which one could hardly conceive of on the basis of the transitory individual relationships as they occur in the usual ward practices of a large institution for mental diseases. Moreover, the patient to patient relationship carries over even into the post-hospitalization existence, as witness the tendency to form ex-patient societies and associations.

In group therapy patients' problems are subjected to a process of intellectualization or objectification. Consciousness and intellect, being a great relaying center between the external world and the more organically associated drives, has an important function in personality homeostasis. Thus, insights acquired in class exert a soft, but steady, pressure.

Usually group psychotherapy is administered by a series of lectures. Believing that in a large mental institution it is necessary to have ready access to a body of information designed to further reeducation and education, even in the academic sense, and recognizing, furthermore, that it may become necessary to change therapeutists on short notice, the author has devised a mimeographed textbook to be used in class. Patients read passages aloud in class and then summarize and comment on what they have read. The therapeutist amplifies and interprets. This frequently leads to interesting digressions, which, in turn, may be the start of symposiums, such as one recently held by a number of patients on the question, "What Is an Open Mind?" Other assignments and book reports are part of the class work. Demonstrations of subject matter are made wherever possible. For example, when the group is studying the chapter on biology, it is taken for a tour of the clinical laboratory and shown slides of tissue cells and germs under the microscope.

The results of group psychotherapy, easily appreciated, are difficult to evaluate objectively in terms of statistics. One reason is that one must abstract qualitatively and quantitatively the spontaneous recoveries and improvements. Second, when, as at the present time, most patients who show any reasonable hope of a favorable outcome are treated with shock therapies, the effects of such treatment must be abstracted from the possible results of group psychotherapy. Nevertheless, in this paper, the author attempted to supply data through clinical cases which not only illustrate improvement with this treatment but demonstrate the operation of some of the major psychodynamics of group psychotherapy.

The New Veteran and the Future for the Practice of Medicine. DR. CONRAD SOMMER, Chicago.

The recent wars in which this country has been engaged were followed by the development of federally controlled and staffed medical programs for the veterans of these wars. This program has been largely centered in the Veterans Administration. The present war will greatly increase the amount of medical practice of this type. The prospect is that upward of 13,000,000 persons will have a right to full hospitalization benefits, both for service-connected illnesses and for any other illness that may develop after the return of the veteran to civilian status.

There is, unfortunately, insufficient closeness of relationship between members of the general medical profession and that part of the profession found in the Veterans Administration.

Physicians, generally, and psychiatrists, in particular, should play a more dynamic role in the care of sick veterans. This enlarged medical role includes a greater use of technics available: occupational therapy, clinical psychology, vocational guidance, recreational therapy, social work and other professional services contributing to the welfare and health of sick persons. The need for fundamental and total rehabilitation of veterans arises from the two serious personality readjustments necessary in moving from civilian to war status and back from combat to peace status.

If the medical profession assumes this dynamic role in the total rehabilitation of veterans, it will gain additional prestige and authority. This may diminish the trend toward socialization of medicine.

DISCUSSION

DR. LLOYD H. ZIEGLER, Wauwatosa, Wis.: This interesting paper points to coming events. I am sure

you would be impressed by a moving picture made in England called "Psychiatry in Action." It demonstrates the methods and facilities used in a densely populated country to restore psychiatric casualties to usefulness.

Men and women have been sensitive about being considered psychiatric casualties. They will continue to be so. It is not difficult to understand why they might seek out the chaplain rather than the physician. There must be teamwork in this whole rehabilitation program, in which the physician, the minister, the business man, the manufacturer, the educator and many others will make up the team.

What is meant by rehabilitation? To me, it is freeing the patient from pain or distress and providing him with opportunities to be as useful as possible in earning a wholesome living for himself and his family. Many of these men will have spent three to five years of their lives in military service, with one or two years in active combat. Let us as physicians condition ourselves to avoid making invalids out of men who have it in them to do better.

The giving of pensions and rehabilitation are not synonymous, by any means. Congress needs much education along these lines. Everything should be done to restore the health and independence of the returning casualties so that they may not be the slaves to disease, attitudes or economic bottlenecks.

Some socialization of medicine, and of other services, may be expected. The leaders in the medical profession should guide this impending change with professional wisdom. As Dr. Sommer has pointed out, the time has come for members of the profession to give up some of their professional isolation and unite wholeheartedly with the many forces of rehabilitation all about them.

Dr. M. T. Koenig, Chicago: I, too, have had experience with the Veterans Administration for many years, and I may say that Dr. Sommer's paper was pleasant but not realistic. He speaks of various facilities for treatment, vocational training and occupational therapy. My experience with veterans of the last war was that they did not want to get well; that is a factor which must be taken into consideration. The veterans who were adequate people to start with have rehabilitated themselves very well, but the majority of those who are still on a pension of the government are men who do not want to get well.

This attitude is fostered in great measure by the various veterans' organizations and by public opinion in general. Dr. Sommer has made some recommendations which sound very good. I, too, should like to make some recommendations. I should like to see a committee investigate the vocational opportunities that were given the veterans in the last war, the cost of these vocational opportunities and the results. After the last war, many of the psychiatrists who were in charge of the various psychiatric hospitals succeeded in getting many of the veterans out of the hospitals by telling them that they could not get paid for their illness. This went on until the veterans' organizations interfered, and then began the milking of the Government. Some of the things they did were simply appalling. For instance, a man who was paid for total disability for life was at the same time employed by a veterans' organization as a liaison officer, with a full salary. I can give a number of such instances. Not only will the veterans not want to get well, but the efforts of well meaning physicians will be frustrated by quasipatriotic organizations who will shout about what terrible experiences the veterans have been through and demand large amounts of money for them. I have seen veterans with diabetes, for instance, who would not enter the hospital unless they could be admitted for a service-connected disability, and they were therefore paid, under pressure of the veterans' organization. We physicians must take into consideration these facts before we make any grandiose plans. Surely, Congress should be educated, but who will sit in Congress? Our intentions are good indeed, but we should not waste our efforts on something that might come to nothing.

Dr. Charles F. Read, Elgin, Ill.: The paper, no doubt, is addressed to members of the medical profession at large and to psychiatrists in particular. Is it not true that the men who return from war activities will be solicitously looked after by the Veterans Administration and by physicians who are working in connection with the Veterans Facilities? Dr. Sommer is apparently trying to show what may be done by the profession at large for the men who will be looked after by the Veterans Facilities. Now, the question is this: How are members of the medical profession in general to get in touch with these men who are going to be given domiciliary care, on the least provocation.

Dr. Ralph Hamill, Chicago: I have watched the service of the Veterans Administration since World War I and have spent two to three mornings a week there for the past twenty-five years. Physicians must be realistic about this problem. They must realize that a certain number of men will be coming back who cannot be satisfied with anything. Are we psychiatrists undertaking to suggest or to state that we can handle this situation? It reminds me of the meetings of the American Psychiatric Association two or three years ago, when the discussion was under way in regard to psychiatrists getting rid of all the unfit. We are told that 30 per cent of the fellows who come back are psychiatric patients. Are we going to cure them? I wonder. I do not mean that we should not make every effort, of course, to help them; but I wonder what we shall be saying ten years from now, and whether many of our efforts will not be frustrated. Some men will want to be cured, and some will not. Some will want the money value, and some will want disability value. I am frankly skeptical of too much expectation on the part of the psychiatrist.

Hemorrhagic Encephalopathy Following Five Day Treatment of Early Syphilis with Massive Doses of Oxophenarsine Hydrochloride (Mapharsen): Report of a Case with Recovery.

Dr. G. Heilbrunn, Manteno, Ill., and Dr. N. L. Hoffenberg, Chicago.

A survey of the literature on hemorrhagic encephalopathy occurring during or after a five day period of treatment with oxophenarsine hydrochloride (mapharsen) reveals a mortality rate of only 25 per cent from that complication, as compared with a fatality rate of 76 per cent for the same mode of administration of other arsenicals. The relative benignness of this complication is confirmed by the case of a 15 year old girl with early syphilis who exhibited typical symptoms of hemorrhagic encephalopathy on the third day after completion of a five day course of treatments, with a total of 1.2 Gm. of oxophenarsine hydrochloride. Final recovery was established nine days after the onset of the cerebral incident.

The role of the therapeutic agents employed was discussed and the use of high doses of ascorbic acid recommended.

In the search for an explanation of the affective selection of this complication, attention was drawn to the psychopathic behavior of the present patient prior to hospitalization and to findings in the literature recording nervous or mental deviations in patients who later had hemorrhagic encephalopathy. It may be tentatively conjectured that a person known to be afflicted with signs of an organic or functional neuropsychiatric disorder may be predisposed to exhibit cerebral complications under the impact of the arsenical drug.

DISCUSSION

DR. C. L. NEYMANN, Chicago: I should like to remind the members of the society of the humane rights of the much abused patient with acute syphilis. After reviewing a great deal of material, involving studies of many thousands of patients. Pusey came to the presumptive conclusion that 55 per cent of all syphilitic patients finally come to some grief as a result of their disease. These patients exhibit serious syphilitic complications years after the infection. However, 45 per cent of all syphilitic patients experience no difficulties late in life provided they are not treated. At present, medicine has entered a period of active arsenical treatment, both with and without fever, of primary and secondary syphilis. Judging from reports that have come to me *sub rosa,* it is clear that some institutions employing massive doses of arsenicals, with and without artificial fever, are abusing rather than aiding the patient with early syphilis. The mortality is too high. A death rate of 3 per cent ascribed directly to treatment of a disease for which the final prognosis may or may not be poor outrages all principles of good therapeutics.

One must bear in mind that it is possible to treat primary and secondary syphilis by means of fever and arsenicals with a minimum of danger. It is also possible to treat patients with latent syphilis in a similar manner. To accomplish this it is necessary to administer average doses of arsenicals combined with fever therapy. Most patients with primary or secondary syphilis can be cured with six artificial fever treatments and six simultaneous injections of 0.3 to 0.4 Gm. of arsphenamine. Such a series of treatments can be completed in three weeks. Why, then, turn to these extremely radical procedures? In addition, the new drug penicillin seems to be efficacious and quite harmless when properly administered. Whether this drug will also prove useful in the treatment of tertiary and post-tertiary syphilis, either in combination with fever therapy or alone, will be determined when larger quantities become generally available. The risk of overwhelming the system with arsenicals does not seem to be justified in treating a disease which is neither immediately fatal nor necessarily disabling to the patient, even after years have elapsed.

DR. J. A. LUHAN, Chicago: I recently had the opportunity to study the brain of a patient who received intensive fever treatment and chemotherapy for syphilis, with a fatal outcome. The patient was a 21 year old healthy Negro with asymptomatic neurosyphilis. He received 150 mg. of insoluble, metallic bismuth intramuscularly the day before the fever treatment, 28.5 mg. of thio-bismol intramuscularly on the morning of this treatment day and then eight hours of fever treatment, during which the rectal temperature remained between 105.6 and 106 F., and the patient received 106.2 mg. of oxophenarsine hydrochloride, in divided doses of 35.4 mg. each. Intermittent confusion developed during the fourth hour of treatment and continued thereafter. The next day impaired renal function was noted, with oliguria and appearance of albumin and granular casts in a urine of low specific gravity, and increasing azotemia. Pneumonia occurred on the ninth postoperative day, which proved refractory to the effects of penicillin and specific type XX antipneumococcus serum. The patient died on the thirteenth postoperative day. Necropsy disclosed confluent bronchopneumonia, affecting all the lobes of the right lung and the upper lobe of the left lung; parenchymatous degeneration of the myocardium; pulmonary edema; toxic changes in the liver and kidneys, and hemorrhagic encephalopathy within the brain. Kodachrome photographs of cut surfaces of coronal slices through the brain and of a cross sectional slice of the midbrain showed the presence of innumerable petechial hemorrhages, particularly throughout the white matter, most of them a fraction of a millimeter in diameter. There were few of these petechiae in the medulla and the cerebellum. A photomicrograph showing several of these petechial hemorrhages revealed ringlike hemorrhages about central areas of seminecrotic brain tissue, in the center of which remnants of capillary structure or a few polymorphonuclear cells could be seen. The central amorphous material was considerably wider than the vessel in its center. No glial proliferation was apparent in the vicinity of these ring hemorrhages. No perivascular round cell infiltrations were found in the brain, and the cerebral cortex was relatively unaffected except for staining alterations of ganglion cells consistent with toxic injury. The pathologic diagnosis of the changes in the brain was cerebral purpura, most pronounced in the white matter of the internal capsule, the midbrain and the pons, and largely sparing the cerebral cortex, the cerebellum and the medulla—a picture consistent with the vasculotoxic effects of an arsphenamine or a chemically related substance.

In this connection, I recall another case of arsphenamine encephalopathy studied at the Cook County Hospital in 1943. A Negro woman of 34, in the fifth month of pregnancy, had received many injections of neoarsphenamine, intermittently, since 1934. Several days after her last treatment convulsions developed, and she was admitted to the hospital in a state of coma. The Wassermann reaction of the spinal fluid was negative. Autopsy disclosed toxic necrosis of the liver, parenchymatous degeneration of the kidneys and bronchopneumonia of the lower lobe of the left lung. The brain revealed a state of hemorrhagic encephalopathy—cerebral purpura, with a larger focus of hemorrhagic encephalomalacia of the corpus callosum. In this case one may speculate whether a marked decrease in the concentration of *l*-ascorbic acid in the blood had not predisposed this pregnant woman to the "allergic" arsphenamine encephalopathy, since Teel, Burke and Draper (Vitamin C in Human Pregnancy and Lactation, *Am. J. Dis. Child.* **56**:1004 [Nov.] 1938) found a notable decrease in the vitamin C content of the blood in a considerable proportion of pregnant women.

It appears that a deficiency of vitamin C leads to a weakening of capillary walls and interferes with the metabolic transfer of hydrogen that depends on the oxidation-reduction system of ascorbic to dehydroascorbic acid. This second function of vitamin C reduces the toxic effect of the arsphenamines by inhibiting their oxidation and thus decreasing their toxic products of oxidation. The pathologic process in arsphenamine encephalopathy (pericapillary encephalorrhagia, as Globus and Ginsburg called it) is dependent on a pri-

mary injury to the capillary structure of the brain, which, for the foregoing reasons, we should expect to be counteracted or prevented in some measure by an adequate concentration of ascorbic acid in the blood. This, and the well documented and astute observations of Dr. Heilbrunn and Dr. Hoffenberg, suggest that every patient about to undergo intensive antisyphilitic chemotherapy be given large amounts of vitamin C and its administration be continued for a number of days after the treatment has been completed.

DAVID SLIGHT, M.D., *President*

Regular Meeting, Oct. 5, 1944

Acute Excitement Induced by Electric Shock Therapy, DR. VERNON L. EVANS, Aurora, Ill.

It has been rather generally thought that electric shock is a fairly harmless form of therapy and that, barring the infrequent physical accidents, the treatment will not make the patient's mental condition worse if it does not help him. However, in a series of 750 patients treated with electric shock at Mercyville Sanitarium, Aurora, Ill., many manifested acute excitement as a result of treatment and 3 died of this cause.

REPORT OF CASES

CASE 1.—A man aged 37, with a condition diagnosed as schizophrenia, simple type, had been ill for two years. The onset was with excitement and overactivity. This condition changed to retardation and uninterest. The patient was retarded, fearful and quiet on entry to the hospital. By the time he had had eleven treatments he was in a state of acute excitement, which persisted and resulted in death three days after the last treatment. Hyperpyrexia (temperature 107.4 F.) developed before death. It appears that this illness began as a catatonic excitement, which became quiescent for two years and was reactivated by the electric shock therapy.

CASE 2.—A man aged 20, with a condition diagnosed as schizophrenia, of undetermined type, had been ill for seven months. At entry the patient laughed and talked to himself and was affable and cooperative, but rather retarded and suspicious. After eleven electric shock treatments he became excited, overactive and delusional. Hyperpyrexia developed, and he died seven days after his last treatment.

CASE 3.—A woman aged 46, with a condition diagnosed as involutional melancholia with schizophrenic features, had been ill for six months. She had been depressed, had threatened suicide and had impulses to harm her husband and her child. She was pleasant and cooperative on admission. She seemed to improve after twelve electric shock treatments. Nine days after the last treatment she showed signs of excitement, and in two or three days this became acute and she expressed absurd delusions. Her excitement continued and progressed, and she died twenty-two days after her last treatment.

CASE 4.—A woman aged 38, with a condition diagnosed as paranoid schizophrenia with depressive features, had been ill for two years. She had "turned against" very close friends. She had been depressed and felt that she had not done her duty. On entry to the hospital she was quiet, cooperative, affable and anxious to please. After twelve electric shock treatments she was grateful and euphoric. A few days after the last treatment she became apprehensive and excited and spoke of dictaphones and people watching through the ventilator in her room. She became out of contact and showed marked increase of psychomotor activity. This condition persisted for many days but gradually quieted, and the patient again became affable, pleasant and cooperative. She returned home and went back to work.

Comment.—These patients were not apparently excited at the time electric shock therapy was started. The excitement developed during or after their course of treatment. The present practice at this institution is to suspend treatments immediately at the first signs of excitement during their course. When the excitement develops several days after the treatments have been finished, the patient is given large doses of sedatives and intensive hydrotherapy at the first signs of this reaction.

Unfortunately, permission for autopsy was not obtained in any of the 3 cases in which death occurred. Many cases of similar "fatal catatonia" in which the patients did not receive shock therapy have been described by numerous writers. When autopsies have been done, the findings have included petechial hemorrhages in the brain and hemorrhages in other areas of the body. It is my opinion that the deaths resulted from the acute excitement and "exhaustion" induced by the electric shock therapy, rather than from a direct traumatic effect of the electric current on the cerebral structures.

The apparent paradox is that electric shock therapy, which acts almost as a specific to quiet acute excitement, induced it in several cases in which it was not present or was quiescent before therapy.

DISCUSSION

DR. C. L. NEYMANN, Chicago: I was interested in this presentation because I have watched and supervised many electric shock treatments. The first question concerned with this treatment is the purpose for which it is administered. It is far too serious a procedure to be used for neuroses or mild psychoses.

The theory, which has been considered seriously as an explanation both of the reaction to electric shock treatment as such and of its success in certain cases, is simple. Perhaps it is too simple. If a person with a psychosis, either functional or organic, is knocked unconscious by a blow on the head, the psychosis will cease from the moment of the blow until the patient recovers consciousness. Now, if a patient is treated every day with electric shock therapy sufficient to produce a convulsion, a deep confusion will soon occur. Later, when he has recovered from the confusion, a retrograde amnesia becomes apparent. This is psychologically similar to the reaction to a mild cerebral concussion.

The psychologic reaction is similar when the patient is treated with insulin or metrazol. The patient in a state of remission after electric shock therapy will always have a retrograde amnesia for the time while he was under treatment. Usually this amnesia extends back several months before treatment was begun. May I be permitted to express the opinion that electric shock treatment should be given at least once a day and should be continued at least to the point at which the patient is totally disoriented for time and place?

Many patients have experienced states of excitement after electric shock therapy. Whenever a state of severe or chronic excitement occurs during the course, it is advisable to give another treatment. This can be

followed by a third, or even a fourth, treatment on the same day. Soon the excitement will cease, as a result of the confusion and amnesia, which are bound to follow.

Let me repeat that treatment of a severe psychosis should not cease until the patient is disoriented for time and place. Even beyond this, his psychic state or mentality should be reduced to a merely vegetative level. He should no longer have control of his urine or feces; he should pay no attention to his food and therefore will have to be fed with a spoon. No matter how deep or how severe the psychosis was, it is nonexistent during this state. Conversely, no matter how great the excitement, this, of necessity, will cease under continued electric shock therapy. Such treatment may even be used to advantage in place of sedation if a patient suddenly becomes violent and unmanageable. Thus, periods of extreme excitement can be overcome with ease.

DR. VERNON L. EVANS, Aurora, Ill.: I knew this paper would bring up questions I could not answer. Of course, it would have been valuable to have had autopsies, but, unfortunately, they were not obtained for any of the 3 patients who died. I know little about pathology; but from what I could read in the literature, most patients who have died of acute excitement without electric shock therapy have displayed these hemorrhagic tendencies and had hyperthermia shortly before death. Autopsy showed these hemorrhages in the brain and in other organs, but these, I gathered, were the main findings, and I think no one was able to connect them directly with the cause of death. Even though there was a mortality rate of nearly 0.5 per cent, I do not feel that this should lead one to discontinue the electric shock therapy. I feel that, while at this institution 1 patient out of 250 has died as a result of the treatment, we have saved many more patients who would have died if they had not received electric shock treatment.

Psychiatric Problems Presented by the Inductee and the Soldier. DR. D. M. OLKON, Chicago.

In summarizing the total effect of army life on the soldier, one cannot escape the conclusion that essential mental factors conducive to mental stability are neither acquired in the milieu nor greatly modified by training and culture. In everyday life a person may get along with faulty mental equipment. Not so, however, in time of severe crisis, such as that experienced in army life, with its inflexible discipline and hazards of war combat. Therefore, in the healthy, steadfast mental equipment of the soldier lies safety and security, and on the psychiatrist rests the responsibility of recognizing and excluding the potentially mental misfit who will handicap army efficiency in time of war and become a liability to society after the war. Moreover, experience in World War I and in the present war seems to establish that once a soldier in the service has a major mental upset the chances for his rehabilitation and return to active duty are very poor.

The presentation was discussed under the following headings: (1) the psychiatric recognition of the unstable personality at the time of induction; (2) the effect of army life on emotionality of the soldier; (3) the effect of combat on an impressionable personality; (4) forced celibacy in army life and its effect on the man in the army; (5) the cumulative effect of strict army discipline; (6) the role of fear of disabilities, disease, difficult climatic conditions, insect pests, etc., in different climes on the mental breakdown of the soldier; (7) the effect of severance of home ties and deprivation of loved ones on the mental organization of the soldier; (8) the scarcity of female companionship and its effect on army morale; (9) malingering, its recognition and evaluation in the inductee and the soldier.

Each item was briefly discussed.

Treatment of mental contingencies in war was not elaborated on. Treatment of war neuroses was discussed in greater detail in a previous publication (*Dis. Nerv. System* **5**:272-277 [Sept.] 1944). Attention was called, however, to certain useless undertakings and lengthy procedures not advantageous in army practice and treatment of war neuroses.

DISCUSSION

DR. C. L. NEYMANN, Chicago: This paper gives a good summary of the various stresses and strains which soldiers must endure in modern warfare. Dr. Olkon has also reviewed the methods to be used in treating patients of this type. I think he struck the right note when he suggested that the psychiatrist should not intrude himself into the patient's personality. This theorem has been accepted by all psychoanalysts and psychiatrists. A great deal can be accomplished by allowing the patient to discuss anything he wishes, without guiding him too rigorously. The crux of the situation may rest on his fears on entering the service, his fears during service, his stresses during service or even his stresses before he entered military life. Such stresses may, and often do, encompass his juvenile and later sexual problems. I think this subject should be a rather open field. The discussion should be directed by the patient, not by the psychiatrist. I am sure we all give our hearty approval to that attitude.

PHILADELPHIA NEUROLOGICAL SOCIETY

GEORGE D. GAMMON, M.D., *Presiding*

Regular Meeting, Oct. 27, 1944

Platybasia (Basilar Impression) Secondary to Advanced Osteitis Deformans (Paget's Disease), with Severe Neurologic Manifestations; Successful Surgical Result: Report of a Case. DR. HENRY WYCIS.

A brief historical résumé of platybasia (basilar impression) was presented.

From the etiologic standpoint, platybasia may be primary (the result of a congenital developmental anomaly) or secondary (the result of bony softening or molding).

A case is reported of platybasia secondary to osteitis deformans, producing severe neurologic manifestations. The patient was treated successfully by high cervical laminectomy combined with suboccipital decompression.

REPORT OF CASE

Mr. R. K., aged 50, was admitted to the neurosurgical service of Temple University Hospital, Jan. 11, 1944.

The patient complained of severe bilateral occipital headaches, bilateral loss of hearing and weakness of the right arm and leg, with dragging of the latter extremity. There were numbness of the right forearm and foreleg, wobbling gait and difficulty in speech, with regurgitation of fluids through the nose. Symptoms began five years prior to admission.

Examination.—The general appearance in the advanced stage of osteitis deformans was striking. The short squat figure, wobbling along with bent shoulders, sunken chest and great head hanging forward, was a living illustration of Sir James Paget's delineation of the disease, in 1876. Movements of the head were limited in all directions. The pupils were equal, but reaction to light was sluggish in the right eye, due to corneal scar. The fundi were normal. Horizontal nystagmus was noted on lateral gaze in either direction. The trigeminal fields were normal for all sensory modalities. The eighth nerve deafness was greater on the right. The gag reflex was present. The tongue protruded in the midline, without tremor or atrophy. There were dysphonia and dysphagia, with nasal regurgitation of fluids.

Gait was markedly ataxic, with dragging of the right lower limb. The Babinski and Hoffmann signs were elicited on the right side, with increased tendon reflexes on this side. The right upper and lower limbs showed marked weakness. There was pronounced dysmetria and dyskinesia of the right upper limb. Hyperalgesia was noted at the level of the second cervical dermatome bilaterally; otherwise sensory disturbances were not distinct.

Laboratory Studies.—The findings were entirely normal except that alkaline phosphatase was elevated to 36 Bodansky units per hundred cubic centimeters of serum.

Roentgenograms.—A block at the foramen magnum was clearly demonstrated. Herniation of the cerebellar tonsils to the level of the upper border of the first cervical vertebra was shown.

Operation.—On January 18, Dr. Wycis did a suboccipital craniectomy with high cervical laminectomy.

Postoperative Course.—The postoperative course was little short of dramatic. There was complete relief of occipital pain and of numbness and tingling of the right arm and leg. Two weeks later the patient felt nearly normal and could walk without ataxia and dragging his leg. There was decided improvement in speech and swallowing. Six weeks later there was little, if any, neurologic abnormality except for an equivocal Babinski sign on the right side.

The author urged neurologic and roentgenographic examinations of the upper cervical portion of the spine and the region of the foramen magnum in all cases of osteitis deformans to disclose the possible presence of platybasia.

DISCUSSION

DR. TEMPLE FAY: Dr. Wycis has demonstrated a case in which decompression in the area of the foramen magnum was followed by dramatic recovery.

In my first case, reported by Dr. W. E. Chamberlain (*Yale J. Biol. & Med.* **11**:487, 1939), the condition was diagnosed by several competent neurologists in this country as multiple sclerosis, syringomyelia or progressive muscular atrophy. On operation, I found compression of the high cervical portion of the cord by a dislocated atlas, although Chamberlain erroneously reported the condition as platybasia.

Since this first case, in which a successful operation was performed five years ago, there have been 19 others in my series, which I reported, with results of operation, before the Society of Neurological Surgeons in Montreal last week. In these cases, like the early ones, symptoms similar to multiple sclerosis or amyotrophic lateral sclerosis were shown. Lesions or compression at the level of the atlas and axis was disclosed in each instance.

Many of these high cervical lesions have been overlooked, I believe, because at autopsy the brain is removed from the skull above the level of the foramen magnum and the cord is usually removed from below, without inspection of the extradural sinuses and the structures around the foramen magnum. The area of the foramen magnum itself, with its relation to the spinal cord, the atlas and the axis, is not deliberately exposed to view by the pathologist at routine autopsy. There is also the difficulty encountered by roentgenologists in visualizing this area. The usual roentgenograms taken of the head or the upper part of the spine do not clearly show the atlas-axis relationship because of the overlying shadows of the mastoid in the lateral view and of the jaw in the anteroposterior view. It is necessary, therefore, to take special stereoscopic roentgenograms, anterior, posterior and lateral, to view this area clearly, and the technic must be concerned with appropriate focal depth and elimination of the overlying and offending structures. This means use of special angles. Such a technic has been developed by Dr. W. E. Chamberlain, at Temple University Hospital; Dr. E. P. Pendergrass, at the Hospital of the University of Pennsylvania, and Dr. C. Carter Hamilton, at the Chestnut Hill Hospital.

With careful roentgenograms, one may easily pick out certain deformities which otherwise would be overlooked. Recent studies have revealed that there is an abnormal anterior displacement of the lamina of the atlas, associated with relaxation of the spinous process of the axis, so that the axis is permitted to be depressed in such a way that the anterior portion of the structure carrying the odontoid process is allowed to angulate backward into the canal. The result of this structural abnormality is that the odontoid process narrows the canal anteriorly and the lamina of the atlas acts to constrict it posteriorly. An actual hourglass appearance has been noted in several instances of so-called amyotrophic lateral sclerosis. This narrowing of the canal interferes with the free venous drainage of the epidural veins, and exploratory laminectomy has revealed not only this constriction and narrowing of the vascular channels, but, when inflammatory reactions are present, enlargement, thrombosis and dilatation of the veins, so that chronic mild compression against the medulla is produced. The pressure anteriorly against the decussation of the motor pathways by the odontoid process may cause spastic paraplegia (primary lateral sclerosis?).

The most common error in diagnosis is to call this lesion "multiple sclerosis." In my experience, two or three clinical points are helpful in making the differential diagnosis between what appears to be diffuse multiple sclerosis and focal high cervical compression of a mild but chronic nature.

There is usually wasting or loss of volume in the muscles of the neck posteriorly. Frequently a distinct change in the perception of cold sense is noted when the sensory status of the area of the trigeminal nerve or the cheek is compared (by stimulation with an ice tube) with that of the second and third cervical dermatomes, below. The use of the ice tube is superior to that of pin prick and other forms of sensory testing, because the patient can, with a fair degree of accuracy, tell the difference in sensory status between the areas in such a way that they may be clearly defined. The second and third cervical dermatomes show various degrees of impairment or hypersensitivity.

My associates and I have observed wasting and atrophy of the intrinsic muscles of the hand in cases of these high cervical lesions, although, according to the textbooks and the prevailing belief, such involvement is ascribed to lower levels of the cord, around the fifth and sixth cervical segments.

When examination reveals the aforementioned deviations from the normal, it has been our custom to order "high cervical roentgenograms," with special reference to stereoscopic visualization of the region of the atlas, axis and foramen magnum.

Although the canal may be found constricted at operation, the result of the Queckenstedt test is usually negative. In my opinion this is due to the fact that the canal is oval at this level, and, although it is compressed anteroposteriorly, there is still space for fluid to transmit pressure along the lateral aspects of the oval.

I am glad to see that Dr. Wycis has added another case to the interesting series of lesions involving this level, which have in the past been so frequently unrecognized or misdiagnosed. Dr. J. J. Keegan, of Omaha, told me recently of 2 cases of so-called multiple sclerosis in which improvement followed high cervical laminectomy, as observed in my first case.

The fact that others are also finding these lesions should stimulate review of the so-called multiple sclerosis group, since neurosurgical intervention in some instances may be of definite benefit.

DR. JOSEPH C. YASKIN: I presume that Dr. Fay does not include among his present series of 19 cases those previously reported before this society. I had the opportunity to observe some of the latter cases later, especially in the wards of the Philadelphia General Hospital. They left me with a rather unpleasant impression, but it is possible that the condition had been neglected and that it was too late for satisfactory surgical intervention.

Dr. Fay's comments regarding the need for caution in diagnosing multiple sclerosis is valid. It is bad practice to make a diagnosis of multiple sclerosis too early or on too little evidence. This is particularly true when there is total absence of involvement of cranial nerves, especially the vestibular and cerebellar pathways and the optic nerves. At best, it is well for the clinician to remember that the diagnosis of lesions in the upper cervical region is at all times very difficult.

DR. HENRY WYCIS: In anticipation of the question whether or not surgical intervention might induce sarcomatous change in bone in Paget's disease, I was informed by Dr. Lawrence W. Smith that he had never encountered such an instance. However, he stated that it was not uncommon for sarcomatous changes to occur in cases of generalized osteitis deformans.

Bruit was not audible in this patient.

I wish to thank Dr. Temple Fay for his excellent discussion of my paper. Dr. Fay has sounded a warning note, and all would profit by remembering it. One should carefully check the sensory levels at the second cervical dermatome in cases of spastic paraplegia diagnosed as multiple sclerosis.

Acute Cortical Blindness with Recovery: Report of a Case.

DR. JOSEPH C. YASKIN and DR. EDMUND B. SPAETH.

Bilateral blindness not infrequently results from bilateral lesions of the media, retina or optic nerve. The neurologic causes of bilateral blindness include bilateral severe retinitis, papilledema, optic neuritis or bilateral optic nerve atrophy associated with infections and neoplastic or traumatic factors. Lesions in the caudolateral angles of the chiasm and the visual radiations rarely cause bilateral blindness except in the region where the calcarine areas approach the poles and lie close to each other. Even here they are relatively infrequent.

C. von Monakow (Die Lokalisation im Grosshirn und der Abbau der Funktion durch kortikale Herde, Wiesbaden, J. F. Bergmann, 1914, p. 331) reported 20 cases of total blindness due to bilateral lesions of the occipital lobe, either from vascular or from infiltrating processes. In many of these cases the disturbance first appeared as a hemiopic defect, followed by complete blindness as a result of involvement of the remaining half field by the pathologic process. Bramwell, Bolton and Robinson (*Brain* **38**:447, 1915) reported a case of blindness from bilateral lesions of the occipital lobe with retention of macular vision as distinct from panoramic vision. Mella (*J. Nerv. & Ment. Dis.* **56**:563, 1922) reported a case of thrombotic cortical amaurosis, the result of the action of methyl alcohol. Marquis (*A. Research Nerv. & Ment Dis., Proc.* **13**:558, 1932), in reviewing the literature, reported 9 cases of complete and permanent blindness, the blindness being caused by vascular lesions in 6 of these cases and by trauma in 3 cases. Two cases were reported by Hemphill (*Irish J. M. Sc.* **181**:28, 1941) in which blindness resulted from occlusion of the basilar artery. Riley, Yaskin, Riggs and Tornay (*New York State J. Med.* **43**:1619 [Sept. 1] 1943) reported 6 cases of blindness from bilateral lesions of the occipital lobes. In 4 of these the blindness was caused by vascular lesions, as verified by autopsy; in 1 case it was due to metastatic carcinoma of the stomach, and in another, to a meningioma. Hamby (*New York State J. Med.* **43**:1632 [Sept. 1] 1943) reported a case of bilateral blindness due to bilateral abscess of the occipital lobe secondary to bronchiectasis.

Cortical blindness is characterized by the absence of changes in the media, retinas or optic disks and by preservation of pupillary reflexes. In some cases central (macular) vision may be retained if the occipital poles have an additional blood supply from the branches of the middle or anterior cerebral arteries. In some cases the visual area is affected primarily by changes in the small terminal vessels. When the blindness is due to slowly developing lesions in the occipital lobes, such as neoplasms or vascular disturbances unaccompanied with other evidences of focal cerebral disease or increased intracranial pressure, the diagnosis may be difficult, and the blindness may be ascribed to psychic causes.

Most cases of cortical blindness terminate fatally by reason of the grave pathologic processes. The recovery in a case is deemed unusual enough to warrant its report.

REPORT OF CASE

M. H., a 48 year old merchant, about the middle of March 1944, had the onset of septic sore throat with acute glomerulonephritis and hypertension. About two weeks later, evidences of a subarachnoid hemorrhage developed, and he became completely blind. The neurologic abnormalities included a rigid neck and a bilateral Kernig sign; there were no other localizing signs. The pupils were large, round and central and reacted promptly to light and consensually. The fundi showed a moderate degree of arterial hypertension, with one small hemorrhage just over the macula of the right eye. In the two weeks following the patient's admission to the hospital, he gradually recovered from the glomerulonephritis and had a satisfactory return of eyesight, without any changes in the retinas.

It was felt that this man had bilateral cortical blindness. Considering the sudden onset, the lesion was probably due to a disturbance of both posterior cerebral arteries or, more likely, of the basilar artery at its bifurcation into the two posterior cerebral arteries. In view of the spontaneous subarachnoid hemorrhage, a rupture of a small aneurysm was deemed a likely process, although emoblism could not be definitely ruled out.

DISCUSSION

DR. HENRY T. WYCIS: Did recovery begin in the macula or at the periphery?

DR. JOSEPH C. YASKIN: I am not certain, but I believe vision first returned in the central field and later extended to the peripheral field. I am reasonably sure that return for form was earlier than that for color. I should like to stress that this case was not one of hysteria and that the patient had pronounced evidences of severe nephritis and subarachnoid bleeding.

Changes in Electrical Activity of the Cortex Due to Applications of Acetylcholine. DR. FRANCIS M. FORSTER and DR. ROBERT H. MCCARTER.

The application of solutions of acetylcholine to the exposed cortices of cats anesthetized with dial produced a period of depression of the cortical activity, followed by cortical discharges. The depression of activity varied in degree in different experiments and extended beyond the area of application of acetylcholine, and even beyond the areas of direct neuronal connection. During the depression of electrical activity, auditory spikes recorded from the auditory receptive areas were decreased or abolished, and responses of the motor cortex to stimulation were decreased or absent.

The discharges following application of acetylcholine varied from short bursts of high voltage spikes, through prolonged bursts of high voltage fast spikes to slow waves of high voltage and some wave and spike formations. These discharges tended to remain localized, but when they spread spontaneously, did so along neuronal pathways. The spread of discharges following application of acetylcholine could be facilitated by the previous application of strychnine.

Immediately prior to and during the period of spontaneous discharge following application of acetylcholine, electrical stimulation of the motor area, auditory stimulation of the auditory receptive area and strychnine firing in any of the areas studied were followed by an acetylcholine discharge if these areas had been the site of application. Stimulation of the motor area under these conditions produced an enhanced response, and previously subliminal stimuli were effective.

From these observations, it is concluded that the application of acetylcholine to the cortex produces a period of depression of electrical activity and a refractory state of the cortex, followed by a localized electrical discharge similar to discharges recorded during clinical seizures. The acetylcholine discharges are spread, either spontaneously or by strychnine facilitation, along neuronal paths.

DISCUSSION

DR. DONALD SCOTT: The authors have shown the greatest care in their technic and preparation and they are to be complimented on the large number of controls by which they have ruled out many complicating factors. I am particularly interested in the reduction of activity that they report, because I wonder whether this might be further investigated by following the temporal spread of such reduction subsequent to the application of acetylcholine. Such a study is perhaps a "shot in the dark" and I don't know whether it would be at all suggestive. I am also interested to know more about the effect of application of acetylcholine to different areas of the cortex, and I wonder whether there was any difference between the two hemispheres which would have any bearing on my question in regard to the spread of this effect immediately following application.

DR. HENRY WYCIS: I should like to ask the authors two questions.

First, do they believe that the action of acetylcholine on the cortex is due to its muscarine-like effect or to a nicotine-like action? In small physiologic doses acetylcholine produces a parasympathomimetic effect, while in large doses it produces a nicotine-like paralysis. Might not the inactivity observed with acetylcholine be due to nicotine-like paralysis? The concentrations used by the investigators here are large, I understand as high as 50 per cent. Other investigators have applied acetylcholine to the cortex in much lower physiologic concentrations, employing as low as 0.2 to 1 per cent; with such concentrations the activity has been nil. I am sure that Dr. Forster is familiar with the work of Chatfield and Dempsey, in which 1 per cent acetylcholine applied to the cortex had absolutely no effect. During increased activity, undercutting the cortex would abolish activity.

Second, in lowering of the blood pressure there is a decrease in the cerebral blood flow. Might not the lowering of the blood pressure with the slowing circulation lead to an accumulation of carbon dioxide, which would, in turn, affect the cortical activity?

DR. GEORGE GAMMON: Is the depression of function which the authors get here related to the concentration of acetylcholine? By starting with a lower concentration, could one skip the depression phase and get stimulation? Also, do the authors consider the action of strychnine similar to the action of acetylcholine? I understand that strychnine binds cholinesterase and that perhaps the two are related.

If I understand their argument, they obtained a discharge in the cortex from acetylcholine which resembled that seen in convulsive seizures, and they therefore suggest that epileptic seizures are due to acetylcholine discharge. Is there any evidence that during such a seizure or during a seizure from electrical stimulation there is any release of acetylcholine, such as occurs from stimulating the vagus nerve supply to the heart?

DR. FRANCIS M. FORSTER: We have not as yet studied the spread of the depression of cortical activity, but we plan to direct our attention in the near future to the further investigation of this phase. We have not encountered difficulty in obtaining adequate acetylcholine responses from the cortex of the parietal or the temporal lobe or from the frontal cortex posterior to the motor area. Area 4, however, frequently produces, after application of acetylcholine, a prolonged period of sharp spikes intermixed with the cortical activity, rather than sharply demarcated bursts of spikes.

Atropinization of the animal does not affect either the period of depression of cortical activity or the subsequent acetylcholine discharges. We varied the concentration of acetylcholine used in these experiments from 1 to 50 per cent in order to determine whether the concentration of the acetylcholine itself was important in the development of the depression or the discharges. We found that the depression of activity occurred when solutions of acetylcholine too dilute to produce discharges were employed. Moreover, the concentration of acetylcholine employed did not alter either the depth or the duration of the depression. The electrical changes of the cortex produced by the application of acetylcholine do not seem to depend on the slight variations in systemic blood pressure, particularly since atropinization abolished these variations.

It does not appear likely that the action of strychnine and that of acetylcholine are entirely similar, since strychnine is said to inhibit cholinesterase, whereas one would expect acetylcholine to be taking part in the enzyme system, including cholinesterase. There is no evidence that there is any release of acetylcholine during an epileptic seizure.

Book Reviews

Large Scale Rorschach Techniques: A Manual for the Group Rorschach and Multiple Choice Test. By M. R. Harrower-Erickson, Ph.D., and M. E. Steiner, M.A. Price $8.50. Pp. 420, with illustrations. Springfield, Ill.: Charles C Thomas, Publisher, 1945.

In the first part of the book the authors deal extensively with the development of the group Rorschach method, stressing its merit as a time-saving device and citing evidence from other investigators as to its value in the classification, selection and screening of maladjusted persons. Adequate directions for administration and for scoring are given, and numerous illustrations appear.

The second part of the book, in which an analysis of the findings of an experimental investigation is presented, is much less convincing, from both the statistical and the clinical viewpoint. The statistical procedure open to most serious challenge is the small and poorly selected sample of subjects used for standardization purposes, involving, as it does, a college group in which more than one half are medical students and nurses. With the individual Rorschach method, such a professional group is generally conceded to report more than the usual number of anatomic responses. The authors recognize the need for contrasting control groups and include them, although a considerable amount of overlapping appears to exist in their choices. Subjects consist of (1) unselected males, (2) patients (psychotic and psychopathic) and (3) two groups of prison inmates, composed of "sex offenders" or persons "serving terms for murder, burglary, grand larceny and forgery." The data do not suggest, however, that in the third group psychopathic personalities have been eliminated.

Little attention is given to the basic problem of reliability of the group method itself, although it appears to be fairly sensitive to variations of administrative technic. Evidence is also lacking that qualitative aspects of the individual Rorschach test principles may not have been altered radically under group conditions. Nevertheless, interpretation is based primarily on principles of the individual Rorschach method, seemingly on the assumption that the two technics reveal personality patterns which are qualitatively similar. If, as the authors suggest, their book is to serve as a "manual" for the group Rorschach method, these theoretic considerations must be met before an adequate evaluation can be made of the method itself. Their statistical tabulation of responses is of value, inasmuch as it constitutes a new and genuine contribution to the literature. To date, no such analysis of responses obtained to the Rorschach cards presented by the group method has appeared.

The multiple choice test, in its original and expanded forms, is described in the third part of the book. The procedure introduces a list of answers for each card against which a subject may check his preferences, and a key is provided for the examiner giving weights to the various responses. The claim is made that this process facilitates not only administration of the Rorschach test, but interpretation as well. Three sections of the book concern themselves with validation of the multiple choice test in terms of its effectiveness in the psychiatric differentiation of military personnel. The contributors, Lieut. Floyd O. Due (MC), U.S.N.R.; Ensign M. Erik Wright, H-V(S), U.S.N.R., and Beatrice A. Wright, Ph.D., present evidence which, although favoring the use of the multiple choice test among trained workers, acknowledges its limitations when employed by persons unskilled in Rorschach interpretation. They qualify their endorsement of the test by stating that their "blind analyses were made from the interpretative principles of the individual Rorschach combined with subjective clinical hunches" (page 214). For a test which purports to objectify and quantify the Rorschach method to a degree which makes it usable by workers untrained in Rorschach interpretation, such evidence is not convincing.

Some of the material in the section on the application of interpretative principles definitely suggests a need for further research. Clinicians experienced in the use of the individual Rorschach method will find it difficult to avoid feeling that much of qualitative significance has been sacrificed, from such statements as the following: "Organic and convulsive states are pooled in this discussion inasmuch as they are indistinguishable interpretively, in the Multiple Choice Test" (page 231), or, "Three case records will be cited to illustrate this group, one with grand mal epilepsy and two cases demonstrating psychiatric evidences of organic intellectual impairment, one with post-traumatic encephalopathy and the other having nervous system syphilis with paresis" (page 232). From their grouping and interpretation, the contributors seem to suggest that organic damage to the brain is to be expected with convulsive disorders, a fact which has yet to be established.

Their conclusions regarding the multiple choice test in general are that "The most accurate inferences of form and degree of maladjustment are possible in the psychoneurotic sub-groups. Organic and convulsive states can be differentiated from other diagnostic categories in a large percentage of cases, but are less accurately specified within the group. Psychopathic personalities can often be recognized by their response patterns. Mental defectives show very abnormal response records, but are not accurately discriminated by this modification of the Rorschach Test" (page 239).

The fourth, and last, part of the book contains classified lists of content obtained from group record responses based on the amplified version of the multiple choice test. This material is definitely of interest, although no conclusions are drawn from group records and no comparison made with individual records taken as a group.

Throughout the entire book, administrative details and appraisal of them are handled by trained Rorschach workers, not by untrained laymen. There is evidence of considerable success with the use of the group Rorschach methods under these conditions. Much, however, remains to be done. In commenting on the book in a recent publication (Rorschach Research Exchange **9**:46-53, 1945), Dr. Marguerite Hertz summarizes its contribution rather well when she says that "'Large Scale Rorschach Techniques' is valuable as a pioneer effort," but that "it is still unsuited for widespread application." Just how far this falls short of the authors' intention is suggested by the publisher's statement on the jacket flap of the book, that the authors

. . . have devised an entirely new test which can be readily used for screening out maladjusted persons by investigation *without extensive training in the Rorschach method.* They present evidence to show that by a simple procedure, taking a few minutes to administer and to evaluate, psychiatrist, psychologist, psychiatric social workers, educator, or counselor may now avail himself of the fruits of research of many years in the Rorschach method."

Many Rorschach workers skilled in the use of the individual method will agree with Dr. Hertz when, in speaking of the group Rorschach and the multiple choice test, she further concludes: "Both tests may be used to advantage only by workers who are steeped in Rorschach methodology, who are willing to subject the tests to thorough study, and to treat their results with suspended judgment." Many will question the wisdom of attempting such oversimplication for the purpose of mass consumption and will regret that such a potentially dangerous weapon has already been placed at the disposal of the novice without proper validation.

The Examination of Reflexes: A Simplification. By Robert Wartenberg, M.D. Price, $2.50. Pp. 222. Chicago: The Year Book Publishers, Inc., 1945.

The primary purpose of this monograph is to simplify the technic and interpretation of reflexes. The author attempts to bring light on the confusing situation which has been produced by the placing of some investigator's name on the reflex obtained by striking a certain part of the body. In this respect he has done a good job. The only adverse criticism of the work lies in the possibility that, in the process of clarifying the situation, the author may lead some readers to believe that the testing of the reflexes is the major part of a neurologic examination. In fact, the author himself states in the preface: "Testing of reflexes and their proper evaluation undoubtedly constitute the most important part of the neurologic examination." Unfortunately, this is the impression of many physicians who are not trained in the intricacies of the anatomy and physiology of the nervous system. To the neurologist, however, the status of either the motor system or the cranial nerves, for example, is of a great deal more importance than the presence or absence of any, or all, of the reflexes. In fact, deviations in the reflexes are usually of no importance except when they are considered in conjunction with the other findings of the neurologic examination.

All of the reflexes are discussed fully, and it is shown that most of the so-called new reflexes are merely old ones elicited by some slight variation in the technic of producing an elongation of the muscle under consideration. The essentials which are necessary to an understanding of the physiology of the reflex and an interpretation of the results are clearly stated in eleven basic principles. These eleven basic principles should be known by every physician who performs a neurologic examination, and they are therefore repeated here in brief. 1. Every striated muscle is capable of contraction on reflex stimulation. The most important reflex stimulus consists of a brief concussion and stretching of the muscle tissue. 2. These muscle stretch reflexes serve as a useful protective mechanism, especially in standing and walking. 3. The strength of the reflex action of the various muscles of any person differs widely, and the strength of the reflex action of any one muscle varies greatly from one person to another. Thus, a lesion of the pyramidal tract may increase existing reflexes and bring latent reflexes to the fore. The appearance of these usually latent reflexes does not mean that the reflexes are new. 4. Since concussion of the muscle and its stretching constitute the true cause of the deep muscle reflex, it is irrelevant whether the concussion comes from the tendon, from the neighboring joint or from bone, or is obtained through mass percussion of the muscle itself. 5. Every muscle crosses one or more joints and is comparable to a tautly drawn bowstring. A muscle reflex may be elicited by tapping on the muscle itself or by stimulation of the convex side of the arch, that is, the bone. 6. Reflex contraction of the muscle can be achieved not only from either side of the bowstring but from neighboring, and even distant, points, with the bone acting as a transmitter of the mechanical insult. Reflexes can be elicited from remote places, particularly where there is functional or organic reflex hyperirritability. The use of the term "extension of the reflexogenous zones" is therefore incorrect. 7. Transmission of concussion through the bone in favorable circumstances may affect several functionally different muscles and thus evoke multiple, but completely independent, unrelated reflexes. One often elicits more than one reflex, the complexity of the response depending on the position of the limb, the strength and direction of the stroke, the relative strength of the reflexes and the degree of general reflex irritability. 8. Each of the clinically important reflexes can be elicited in normal persons in three, four, or even more, ways. A boundless confusion results in giving a special, or even a proper, name to each way of eliciting a single reflex. The chief focus of attention should be on the muscle whose action is provoked and not on the point of elicitation of the reflex. 9. Reflexes are the result of concussion and stretching of muscles, and the use of such terms as tendon, bone, periosteal, osteoperiosteal, osteotendon, joint, fascial or aponeurotic reflexes is misleading. 10. There is no justification for the use of the term "paradoxic" or "antagonistic" reflex. These phenomena are simply occasional forms of well known deep reflexes appearing under certain conditions and depending on particular technics applied in their elicitation. They are easily understandable, normal phenomena. 11. The second large group of reflexes are called superficial, or "skin," reflexes. In the superficial reflex, a stimulus applied to the skin evokes the reflexive contraction of the muscle. It is an indirect muscle reflex. Superficial reflexes differ from deep reflexes in that they are evoked by a greater variety of stimuli; their zone of excitation is much more extended; their latent period is longer, and their fatigability is greater. Whereas every muscle has its deep muscle reflex, only a few muscles have their superficial reflexes as well.

The Story of a Hospital. By Charles A. Elsberg, M.D. Price, $3.50. Pp. 174. Paul B. Hoeber, Inc., 1945.

Dr. Elsberg has given an accurate account of the development of the Neurological Institute. He carries one fluently and with easy motion through the tumultuous vicissitudes of its early years: that period of crystallization and growth of the organization which has attained a place of distinction in the medical annals of New York.

He describes with simple clarity the labor and devotion of the founders, both lay and medical, and tells how the indomitable energy of two medical men by procuring funds galvanized the board of directors into securing the incorporation, the purchase of the old building and the organization of the hospital as an entity.

One could wish he had drawn a more graphic picture of those early days, with more details of the inevitable clash of strong dominant personalities, the confusion of the clinic afternoons, when the traffic lines of patients bound for the physical therapy department became jammed with the lines of clinic patients going to be examined, and the ease with which this tangle was always rectified by one small, calm, efficient nurse. A striking picture of the line of applicants waiting for admission to the outpatient department, which often reached more than halfway down the block, might have been added, as well as a mention of the flexibility of the administration, whose ingenuity in wangling additional space for the expanding activities of new departments seemed unbounded. To those of us who participated in this period, these details form a pleasing section of a mosaic that is an integral part of the early history of the Institute.

The story of the reorganization which resulted in a new building and coalition with the Columbia-Presbyterian Center is well told, although the author is somewhat modest about the part he played in this development.

The account of the final amalgamation with the Presbyterian Hospital and the subsequent reorganization signalizes another milestone in the progress of the Institute and contains illuminating details of the changes in the various departments and the closer coordination with the staff of the Presbyterian Hospital. The closing chapter takes cognizance of the fact that the Institute is weathering a second world war, which, while absorbing many of its staff for the armed forces, has not stripped it to the bone, as was the case in World War I.

Dr. Elsberg in the closing chapter yields to the temptation to philosophize in his gentle way on the cataclysmic throes of the world today. He takes issue with the pessimistic views of Bertrand Russell concerning the future of mankind and gives in outline an ethical formula for the establishment of a lasting peace.

The Cultural Background of Personality. By Ralph Linton, Ph.D., Professor of Anthropology, Columbia University. Price, $1.50. Pp. 153. New York: D. Appleton-Century Company, Inc., 1945.

This book was written as an outgrowth of a series of lectures delivered by the author on the general subject of the interrelations of culture, society and the individual. Dr. Linton recognizes the necessity for the collaboration and utilization of many technics in the study of personality. He seeks the cooperation of psychology, sociology and anthropology. He should have included also anatomy and physiology.

In this small book are packed a wealth of information and an honest appraisal of what has been accomplished in the field of personality by the social sciences to date. The psychiatrist can read with profit the general concepts of the anthropologist. What is more, there appears a discussion of the shortcomings as well as the advantages of the anthropologic technic.

The chapters on the concept of culture and the one on personality are particularly good. The organization and classification of material provide in condensed form a quick orientation for the reader and give him a point of view which stresses the all-pervading factor of society, of culture, of environment on personality evaluation. For example, the author redefines neurosis as "an individual value-attitude system not shared by other members of society" which the individual expresses "in specific overt responses not adjusted to his cultural and social milieu." He agrees that the first few years of life are crucial for the establishment of the highly generalized value-attitude systems which form the deeper levels of personality content.

Dr. Linton concludes that culture is the main factor producing "normal" personality in any group. However, he states that the causes of aberrant personality are still imperfectly understood.

This book is highly recommended.

News and Comment

AMERICAN SOCIOMETRIC ASSOCIATION

An American Sociometric Association has been founded, and its first officers were elected by means of a sociometric poll. Officers of the association are: president, J. L. Moreno; secretary, Helen H. Jennings; treasurer, George A. Lundberg; counselors, Gardner Murphy, Ronald Lippitt and Zerka Toeman.

The association has at this time 100 charter members and 175 new applicants for membership. The aim of the association is to provide a meeting point for the various social science associations as a center in which their mutual research interests can be promoted. Its charter membership consists of a cross section of sociologists, psychiatrists, psychologists, anthropologists, social workers and so forth.

Annual membership fee is $5, including subscription to the journal *Sociometry*. Communications and applications for membership may be addressed to: American Sociometric Association, Room 327, 101 Park Avenue, New York 17.

AMERICAN PSYCHIATRIC ASSOCIATION

The American Psychiatric Association is desirous of being of service to its members and to other physicians interested in psychiatry. The association is particularly interested in making available "refresher courses" of about three months and fellowships or residencies of a year or more. In order that appropriate plans may be made, it is urgently requested that physicians now in the armed forces who wish to avail themselves of such opportunities communicate with the secretary, Dr. Winfred Overholser, Saint Elizabeths Hospital, Washington 20, D. C., indicating their desires.

CORRECTION

In the article by Dr. Silvano Arieti entitled "Primitive Habits and Perceptual Alterations in the Terminal Stage of Schizophrenia," in the May issue (ARCH. NEUROL. & PSYCHIAT. **53**:378, 1945), second column, page 381, the last word in the third from the last line of the first paragraph should be "lobotomy" instead of "lobectomy."